

Journal of Indian Physician Associates

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Table of Contents

Original Research Article

- 1** Randomized Controlled Trial Comparing Endoscopic and Open Vein Harvesting: Histologic Assessment of Distended and Nondistended Saphenous Vein 1
Sam Raaj; William R. Critchley, PhD; Nehru Devan, MSc; Janesh Nair, MA; Muhammad Khawaja, MBBS; Stuart Grant, PhD; Azita Rajai, MSc; James B. Barnard, MD; Bhuvaneswari Krishnamoorthy, MSc, PhD

Review Article

- 2** Ex Vivo Lung Perfusion in Lung Transplantation: Clinical Impact and Expanding Horizons 12
Anitha Chandrasekhar, DMSc; Chitaru Kurihara, MD; Ankit Bharat, MD

Narrative Reviews

- 3** Current Trends in Coronary Artery Bypass Grafting - Innovations Shaping Modern Coronary Revascularization 20
M. Arockia Grazy, BS-PA, MBA
- 4** Sprays, Injections, and Topical Therapy: Are Vaccines on the Horizon for the Treatment of Recurrent Urinary Tract Infections in the United Kingdom? 27
Chandran Louis, BSc Hons PgDip, SFHEA; Amy Donaldson-Perrott, BSc Hons PgDip, SFHEA; Chanceeth Chandrakanthan, BSc Hons PgDip, SFHEA
- 5** Towards a Globally Recognized Physician Associate Role: Standardization, Disaster Readiness, and Systems Integration 32
Bryn L. Kroto, DMSc, PA-C; Bianca R. Wesbrook, DMS, PA-C; Richard Gilbert, DMS, PA-C

Narrative review with comparative health systems analysis

- 6** The Symphony of Care: Physician Associates Multifaceted Role in Extracorporeal Membrane Oxygenation Program 40
Jumana Yusuf Haji, MD; Dinesh Kumar Kandavel, BS-PA, PGDM HCM

Narrative review - Commentary

- 7** Immunization System Resilience and Measles Outbreak Prevention: A Narrative Review of India and Bangladesh 47
Monika Kochar, BDS, MPH

Case Report

- 8** Minimally Invasive Redo Mitral Valve Replacement After Prior Annuloplasty Ring Repair 54
Satyajit Patra, BSc-PA; Binay Krishna Sarkar, MS, MCh, DNB, MRCSE, MNAMS, FIACS; Mondira Mondal, BSc-PA; Biswajit Mondal, BSc-PA

From the Editor's Desk



Gratitude • Grace • Grit • Growth

Dear Readers, Colleagues, and Friends of the Physician Associate Profession,

It gives me immense pleasure to welcome you to the *September 2026* issue of the *Journal of the Indian Physician Associate Association (JIPA)*.

This edition is particularly special to us. We bring it to you ahead of schedule, with seven research-oriented, data-driven contributions that reflect a profession increasingly finding its voice through evidence, clinical experience, and academic inquiry.

This issue also arrives at a significant moment for our profession. As we look forward to National Physician Associate Day in October and the historic IAPACON–GACOPA International Conference being hosted jointly in India, it is an opportune time to pause and reflect—not merely on where the Physician Associate profession stands today, but on how far it has travelled and where it must go next.

A Profession Born Out of a Healthcare Need

At its heart, the Physician Associate profession was never created simply to add another designation to healthcare.

It emerged from a fundamental question: How do we extend the reach of medicine to patients who need it most?

From the *Barefoot Doctors* of rural China in the 1960s to the pioneering work of Dr. Eugene Stead Jr., who established the first formal Physician Assistant programme at Duke University in 1965, different healthcare systems arrived at variations of the same answer—appropriately trained clinical professionals can extend the capacity of doctors and make healthcare more accessible.

The profession subsequently evolved across countries and healthcare systems, including the United Kingdom, adapting itself to the changing needs of modern medicine.

Its underlying principle, however, remained remarkably constant: Team-based healthcare, where every trained professional contributes meaningfully to patient care.

From the Clinic to the Operating Room

The contribution of Physician Associates has never been restricted to primary care.

In surgery, particularly in high-complexity specialties, PAs have increasingly become an integral part of the clinical team—contributing to procedural continuity, perioperative care, technical assistance and the standardisation of surgical workflows.

The history of medicine also reminds us that major advances are rarely the work of one individual alone. The story of Vivien Thomas, who worked alongside Dr. Alfred Blalock in developing and perfecting the Blalock–Taussig shunt, is a powerful reminder of the importance of skilled technical expertise, innovation and collaboration in surgical progress.

His contribution challenges us to look beyond titles and recognise the knowledge, skill and dedication of every member of the healthcare team.

The evolution of minimally invasive procedures, endoscopic conduit harvesting, robotic surgery, arthroplasty pathways and increasingly sophisticated perioperative systems further demonstrates how modern medicine depends upon well-trained, specialised teams working together with precision.

The lesson is simple:

Modern healthcare is not built around individuals. It is built around teams.

The Indian Opportunity

For India, this conversation assumes an even greater importance.

Our healthcare system faces enormous geographical, demographic and workforce challenges. The burden of disease is rising, chronic illnesses require long-term follow-up, emergency departments remain crowded, and specialist expertise is unevenly distributed across urban and rural India.

This is where the Physician Associate can become a meaningful force multiplier.

A well-trained PA can contribute to routine clinical assessment, chronic disease follow-up, triage, emergency stabilisation, perioperative care, preventive health programmes and telemedicine-enabled services—always as part of a structured healthcare team and within an appropriately defined scope of practice.

The opportunity is not to replace the physician. The opportunity is to enable the physician to do more.

If appropriately integrated, PAs can help specialists focus their time and expertise where it is most needed—while ensuring that patients receive continuity of care throughout the healthcare journey.

From Workforce Expansion to Professional Standards

As the profession develops in India, however, growth must go hand in hand with responsibility.

The *National Commission for Allied and Healthcare Professions (NCAHP)* framework represents an important step towards standardisation, education, registration and professional accountability.

Recognition brings with it an equally important obligation: quality.

The future of the profession cannot be built on informal titles, inconsistent training or unregulated practice. It must be built on properly educated, appropriately qualified and professionally accountable Physician Associates.

Our patients deserve nothing less.

Hospitals and academic institutions must therefore recognise the distinction between a formally trained Physician Associate and individuals working without standardised professional education or accreditation.

Professional recognition must ultimately translate into patient safety, clinical competence and public trust.

Why Research Matters for PA Professionals

This brings me back to the present issue of JIPA. A profession matures when it begins to document its own experience. Clinical practice gives us experience. Research gives us evidence. Academic discourse gives us direction.

The seven contributions in this issue represent more than individual papers. Together, they reflect a profession that is beginning to ask important questions, examine its own practice and contribute to the larger body of healthcare knowledge.

This is precisely the culture we must encourage.

We need more research.

We need stronger academic collaborations.

We need multicentric studies.

We need outcome-based evidence.

And, most importantly, we need to create a culture in which Physician Associates are not merely participants in healthcare delivery, but contributors to the evidence that shapes healthcare delivery.

Selected Landmark Physician Associate/Assistant Research — 2016–2026

No.	Paper & Citation	Journal / DOI	Scientific Takeaway
1	Halter M, Wheeler C, Pelone F, et al. <i>Contribution of physician assistants/associates to secondary care: a systematic review.</i>	BMJ Open. 2018;8:e019573. DOI: 10.1136/bmjopen-2017-019573 (PubMed Central (PMC))	Systematic review of 16 studies across emergency medicine, trauma & orthopaedics, acute medicine and mental health. PAs were associated with improved waiting times, throughput and continuity, with little evidence of adverse effects on patient outcomes or costs. (BMJ Open)
2	Hooker RS, Moloney-Johns AJ, McFarland MM. <i>Patient satisfaction with physician assistant/associate care: an international scoping review.</i>	Human Resources for Health. 2019;17:104. DOI: 10.1186/s12960-019-0428-7	International evidence demonstrated generally high patient satisfaction with PA care. Patient acceptance was influenced by understanding of the PA role and effective integration within the healthcare team.
3	Lack A, Saddik M, Engels P, Lethbridge S, Nenshi R. <i>The emergence of the physician assistant role in a Canadian acute care surgery setting.</i>	Canadian Journal of Surgery. 2020;63:E442–E448. DOI: 10.1503/cjs.002119	Demonstrated substantial PA participation in acute-care surgery, including patient encounters and multidisciplinary activity. Provides quantitative evidence for the PA as a continuity professional within a surgical team.

No.	Paper & Citation	Journal / DOI	Scientific Takeaway
4	van den Brink GTWJ, Hooker RS, Van Vught AJ, Vermeulen H, Laurant MGH. <i>The cost-effectiveness of physician assistants/associates: a systematic review of international evidence.</i>	PLOS ONE. 2021;16:e0259183. DOI: 10.1371/journal.pone.0259183 (PLOS)	Review of 39 comparative studies. In 29 studies, PA care had lower labour/resource costs; quality was comparable in 15 studies and better in 18. The evidence supports PAs as a potentially cost-efficient component of healthcare delivery, while recognising methodological limitations. (PLOS)
5	Katz J, Powers M, Amusina O. <i>A review of procedural skills performed by advanced practice providers in emergency department and critical care settings.</i>	Disease-a-Month. 2021;67:101013. DOI: 10.1016/j.disamonth.2020.101013	Reviewed procedural practice among advanced practice providers, including PAs, in emergency and critical care. Highlights the expanding role of PAs in procedural medicine and acute care, alongside the need for structured competency-based training.
6	Huang C, Morone C, Parente J, et al. <i>Advanced practice providers proficiency-based model of ultrasound training and practice in the ED.</i>	JACEP Open. 2022;3:e12645. DOI: 10.1002/emp2.12645	Demonstrated a structured, proficiency-based approach to point-of-care ultrasound training for advanced practice providers. Illustrates the transition from role-based training to objective competency and skills assessment.
7	Halvachizadeh S, Goezmen S, Schuster S, et al. <i>The implementation of physician assistant in a surgical ward improves continuity in daily clinical work and increases comprehensibility of nurses and physicians.</i>	Patient Safety in Surgery. 2022;16:34. DOI: 10.1186/s13037-022-00344-7	PA integration into a surgical ward improved continuity of daily clinical work and communication between nurses and physicians. Demonstrates that PA contribution can be system-level, improving team function rather than simply substituting for individual physician tasks.
8	King NMA, Habeeb M, Helps S. <i>The contribution of physician associates or assistants to the emergency department: a systematic scoping review.</i>	JACEP Open. 2023;4:e12989. DOI: 10.1002/emp2.12989	Synthesised evidence on PA contribution to emergency departments, including waiting times, length of stay, patient outcomes, satisfaction and team perceptions. Emergency medicine emerges as one of the most extensively studied environments for PA integration.
9	DePalma SM, Hooker RS, Bruza-Augatis M, Kozikowski A, Puckett K. <i>Demographics and Characteristics of Cardiology Physician Assistants/Physician Associates in the United States: A Workforce Analysis.</i>	JACC: Advances. 2024;3:101394. DOI: 10.1016/j.jacadv.2024.101394	Provides contemporary data on the PA workforce in cardiology, illustrating the increasing specialisation of the profession and its integration into cardiovascular care. Particularly relevant to cardiovascular and surgical PA practice.
10	Cooper N, Agius S, Freeman K, et al. <i>Impact of physician assistants on quality of care: rapid review.</i>	The BMJ. 2025;390:e086358. DOI: 10.1136/bmj-2025-086358	One of the most recent major evidence syntheses. Comparative studies generally support safe and effective PA practice, particularly with appropriate supervision and in post-diagnostic care. Importantly, it also highlights the need for better prospective and comparative research.

A Profession Increasingly Defined by Evidence

The last decade has also witnessed an important transformation in Physician Associate scholarship. The profession is no longer described merely through workforce numbers or anecdotal experience; an expanding body of peer-reviewed research now examines its contribution to patient care, emergency medicine, surgery, education, economics and health-care systems.

Systematic reviews published in *BMJ Open*, *Human Resources for Health*, *PLOS ONE*, *JACEP Open* and, most recently, *The BMJ* have examined the contribution of Physician Associates to secondary care, patient satisfaction, cost-effectiveness, emergency medicine and quality of care. Individual studies from Canada, Switzerland and the United States have further demonstrated measurable contributions to acute-care surgery, surgical ward continuity, point-of-care ultrasound and specialty practice.

The message emerging from this literature is neither that Physician Associates replace physicians nor that every PA model is equivalent. Rather, the evidence increasingly supports a more nuanced proposition:

“appropriately educated and credentialed Physician Associates, working within clearly defined scopes and integrated into physician-led multidisciplinary teams, can expand healthcare capacity, improve continuity and contribute meaningfully to patient care”

Equally important, the literature reminds us of our responsibility. Much of the existing evidence remains observational, heterogeneous and concentrated in a handful of countries and specialties. The next decade must therefore be an era of stronger prospective studies, multicentre research, patient-outcome research and health-economic evaluation.

For the Physician Associate profession in India, this is perhaps our greatest opportunity. We should not merely import the evidence generated elsewhere; we must generate our own.

India needs Indian data, Indian research questions and Indian outcomes.

The future of the profession will ultimately be secured not by assertion, but by evidence.

Looking Forward

As we celebrate National Physician Associate Day and gather for the historic IAPACON–GACOPA joint conference in India, I believe we are standing at an important crossroads.

The next chapter of the Physician Associate profession in India will not be defined merely by numbers or recognition.

It will be defined by competence, credibility, research, professionalism and the value we bring to our patients and our healthcare teams.

JIPA hopes to be a part of that journey.

Through this journal, we seek to create a platform where clinical experience can become academic knowledge, where questions can become research, and where evidence can ultimately influence policy and practice.

I invite our readers—clinicians, academics, educators, students, researchers and healthcare leaders—to engage with the work presented in this issue, question it, build upon it and contribute to the conversation.

The future of the Physician Associate profession will not be written by a few individuals.

It will be written collectively—through our clinical work, our research, our integrity and our commitment to patients.

Let us therefore continue to document our evidence, celebrate our contributions and, most importantly, remain worthy of the trust that patients place in the healthcare professionals who care for them.

The journey has begun. The responsibility is ours.

Sincerely,

Ashish Gaur

Editor-in-Chief

Journal of Indian Physician Associates (JIPA)

Joint Secretary, IAPA

Senior Surgical Associate/Senior Manager

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Sir HN Reliance Hospital, Mumbai

From the Co-Editor-in-Chief



It is with great pleasure that I welcome you to the second volume of the Journal of International Physician Associates (JIPA).

The journey of JIPA since the launch of our inaugural issue in October 2025 has been both encouraging and rewarding. In a relatively short period, the journal has made significant progress in establishing itself as an international platform for knowledge sharing, clinical scholarship, research, and professional dialogue. The growing interest and contributions from colleagues across different countries are a testament to the evolving role of Physician Associates and the need for a dedicated platform that reflects this progress.

This second volume brings together a diverse range of original research, reviews, case reports, and professional perspectives, reflecting the breadth of contemporary clinical practice and the expanding contribution of Physician Associates within multidisciplinary healthcare teams. The content spans innovative clinical approaches, advances in diagnosis and treatment, emerging healthcare technologies, and important discussions surrounding the development and integration of the Physician Associate profession.

Beyond the individual articles, this issue represents what we hope JIPA will continue to stand for — evidence-based practice, professional development, international collaboration, and the sharing of experiences that can contribute to better patient care and stronger healthcare systems.

As the Physician Associate profession continues to develop across different parts of the world, we believe that JIPA has an important role to play in documenting this journey, providing

a platform for diverse voices, and encouraging meaningful academic and professional exchange. Our aspiration is that, in the coming years, JIPA will grow into a leading journal for Physician Associates globally and a respected publication within the wider healthcare community.

The successful publication of this volume would not have been possible without the collective efforts of many individuals. I would like to extend my sincere gratitude to our Editorial Team, reviewers, authors, contributors, and everyone working behind the scenes who have dedicated their time, expertise, and enthusiasm to the continued growth of JIPA.

We are grateful to everyone who has believed in the vision of this journal and supported us since its inception. As we move forward, we remain committed to maintaining the quality and relevance of JIPA while creating greater opportunities for Physician Associates and healthcare professionals around the world to share, learn, collaborate, and contribute.

I hope you enjoy this issue and find it both informative and inspiring.

Sincerely,

Dr. Tanmay Acharia, DMSc

President, IAPA

Co-Editor in Chief

Journal of Indian Physician Associates (JIPA)

Senior Surgical Associate/Team Leader

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Meril

More to Life

ADDING MORE TO LIFE..



Research Empowering Individual

Randomized Controlled Trial Comparing Endoscopic and Open Vein Harvesting: Histologic Assessment of Distended and Nondistended Saphenous Vein

Sam Raaj¹; William R. Critchley²; Nehru Devan³, Janesh Nair³, Muhammad Khawaja³; Stuart Grant³; Azita Rajai⁴, James B. Barnard³, Bhuvaneswari Krishnamoorthy^{3,5,6}

Abstract

Introduction: Vein graft injury promotes intimal hyperplasia, luminal narrowing and thrombosis. Surgical trauma during harvesting, including distension and handling, induces smooth muscle cell migration and intimal thickening. However, the structural impact of harvesting techniques remains unclear. We evaluated structural damage and distension-related changes in saphenous veins harvested using 3 techniques.

Methods: A total of 300 patients were randomly assigned to open vein harvesting (OVH), closed tunnel endoscopic vein harvesting (CT-EVH), and open tunnel endoscopic vein harvesting (OT-EVH). A 1-cm vein sample was collected from the proximal region (undistended, $n = 300$), the distal (distended with 20 mm Hg pressure, $n = 300$), and a random sample (underwent surgical trauma, 70 mm Hg pressure cardioplegia and distension, $n = 300$). Picrosirius red staining ($n = 900$) was used to assess the structural integrity of the vein wall, including the longitudinal smooth muscle layer and collagen architecture. Five independent researchers and a histopathologist, blinded to group allocation, scored all specimens.

Results: Intimal disruption was greatest in the OT-EVH group across proximal, distal, and random samples (all $P < 0.001$). Medial layer disruption was highest in CT-EVH, whereas OVH demonstrated the least disruption in all regions (all $P < 0.001$). Internal muscle migration was significantly greater in OT-EVH compared with other groups (all $P < 0.001$). Circular smooth muscle detachment was more frequent in endoscopic groups than OVH in proximal ($P = 0.008$), distal ($P < 0.001$), and random samples ($P = 0.001$). Longitudinal layer detachment was similar in proximal ($P = 0.113$) and distal ($P = 0.380$) samples but greater in endoscopic groups in random segments ($P = 0.012$).

Conclusion: OVH preserved saphenous vein structural integrity better than EVH techniques. Among EVH techniques, OT-EVH was associated with the greatest intimal disruption, affecting both nondistended and distended segments, with more pronounced disruption observed in distended and manipulated segments. In contrast, CT-EVH demonstrated greater medial injury. These differential injury patterns may reflect the effects of harvesting technique, including tunnel creation, traction, and tissue manipulation, and highlight the importance of technique and device selection in preserving conduit integrity.

Trial Registration: ISRCTN Registry identifier: ISRCTN91485426

Keywords Coronary artery bypass surgery, open vein harvesting, endoscopic vein harvesting, muscle migration, intimal stretching

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Introduction

Coronary artery disease (CAD) is managed with percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), with treatment selection guided by anatomic complexity, lesion severity, and comorbidities such as diabetes mellitus.¹ In patients with multivessel CAD, evidence indicates superior cardiac outcomes and a potential long-term survival benefit with CABG compared with PCI.² National registry data demonstrate that the left internal thoracic artery in combination with the long saphenous vein (LSV) remains the predominant conduit strategy, with more than 90% of CABG procedures in the United States and Canada using this configuration, as reported by the Society of Thoracic Surgeons database.³ The LSV continues to be widely used in multiple bypass grafting owing to its accessibility and adequate length.⁴

Minimally invasive vein harvesting techniques have been increasingly adopted to reduce wound complications and postoperative morbidity associated with traditional open vein harvesting (OVH).⁵ However, the LSV exhibits higher rates of early and late graft failure compared with arterial conduits, reflecting inherent anatomic and physiologic differences.⁶ Endothelial injury sustained during harvesting, particularly disruption of the vasa vasorum and perivascular nerves within the adventitia, represents a key contributor to early vein graft failure.^{7,8} Despite reduced wound morbidity, the use of endoscopic vein harvesting (EVH) remains controversial because of concerns regarding conduit integrity and graft quality. Several strategies have been proposed to enhance LSV preservation and long-term patency, including the no-touch harvesting technique,⁹ minimization of mechanical manipulation,¹⁰ and application of external venous support stents.¹¹

Vein graft failure remains a major limitation after CABG and is influenced by harvesting technique, intraoperative distension, preservation methods, and coronary target vessel quality, culminating in intimal hyperplasia, luminal narrowing, and thrombus formation.^{12,13} Experimental and clinical evidence indicates that mechanical trauma sustained during harvesting, together with excessive distension and manual handling, promotes smooth muscle cell migration, resulting in intimal thickening and proliferative remodeling.¹²⁻¹⁵ In addition, endothelial denudation impairs conduit function through reduced release of prostacyclin and endothelium-derived relaxing factors, mechanisms implicated in the pathogenesis of early graft failure.^{8,16,17}

Methods

Study Design

Between 2011 and 2015, 300 patients undergoing CABG were randomized into 3 groups. This study represents a predefined

subanalysis of the Vein Integrity and Clinical Outcome (VICO) trial⁵ designed to evaluate the effects of distended and nondistended vein samples across 3 vein harvesting techniques.

The VICO trial was registered on the Integrated Research Application System trial registry before commencement of recruitment and additionally registered on the International Standard Randomised Controlled Trial Registry (ISRCTN91485426) in accordance with European Union regulation 536/2014. The full study protocol has been published as part of the main study results of the VICO trial.⁵

Simple block randomization was performed by an independent statistician. Allocation concealment was ensured using sequentially numbered, opaque, sealed envelopes prepared by an independent research assistant responsible for the allocation sequence. Patients were randomly assigned to 3 harvesting techniques. Therefore, the influence of patient-specific characteristics on histologic outcomes was not examined.

All vein conduits were harvested by surgical practitioners who had each completed at least 250 procedures with their respective harvesting technique before study commencement. This prerequisite was intended to minimize the influence of the learning curve on histologic outcomes. The study was not designed to evaluate changes in histologic findings according to increasing operator experience over time. A total of 900 vein samples were collected (Figure 1). Samples were classified as H1 (nondistended proximal segment), H3 (distended distal segment following 20 mm Hg flush to assess leakage using VasoShield pressure syringe [Getinge]), and H2 (segment obtained after surgical manipulation, 70 mm Hg cardioplegic flush pressure and distension).

Group 1 – (Control arm): 100 patients undergoing OVH.

Group 2 – (Intervention 1): 100 patients undergoing closed tunnel endoscopic vein harvesting (CT-EVH).

Group 3 – (Intervention 2): 100 patients undergoing open tunnel endoscopic vein harvesting (OT-EVH).

All histologic specimens were scored in a blinded manner by 5 independent assessors and a consultant histopathologist.

Surgical Techniques

Both OVH and EVH were performed according to previously described techniques.^{5,18} The site and harvest length for LSV harvesting was determined by the number of conduits required. This may influence comparability between segments. When 1 to 2 conduits were required, the vein was retrieved from the midcalf to the thigh, whereas when 3 lengths were required, harvesting was extended from the ankle to the thigh. In the OVH group, the vein was retrieved via a longitudinal leg skin incision either from the midcalf or from 2 cm above the medial malleolus. All veins were harvested with surrounding perivascular adipose tissue preserved. Side branches were ligated using 4-0 Vicryl ties and metal ligaclips.

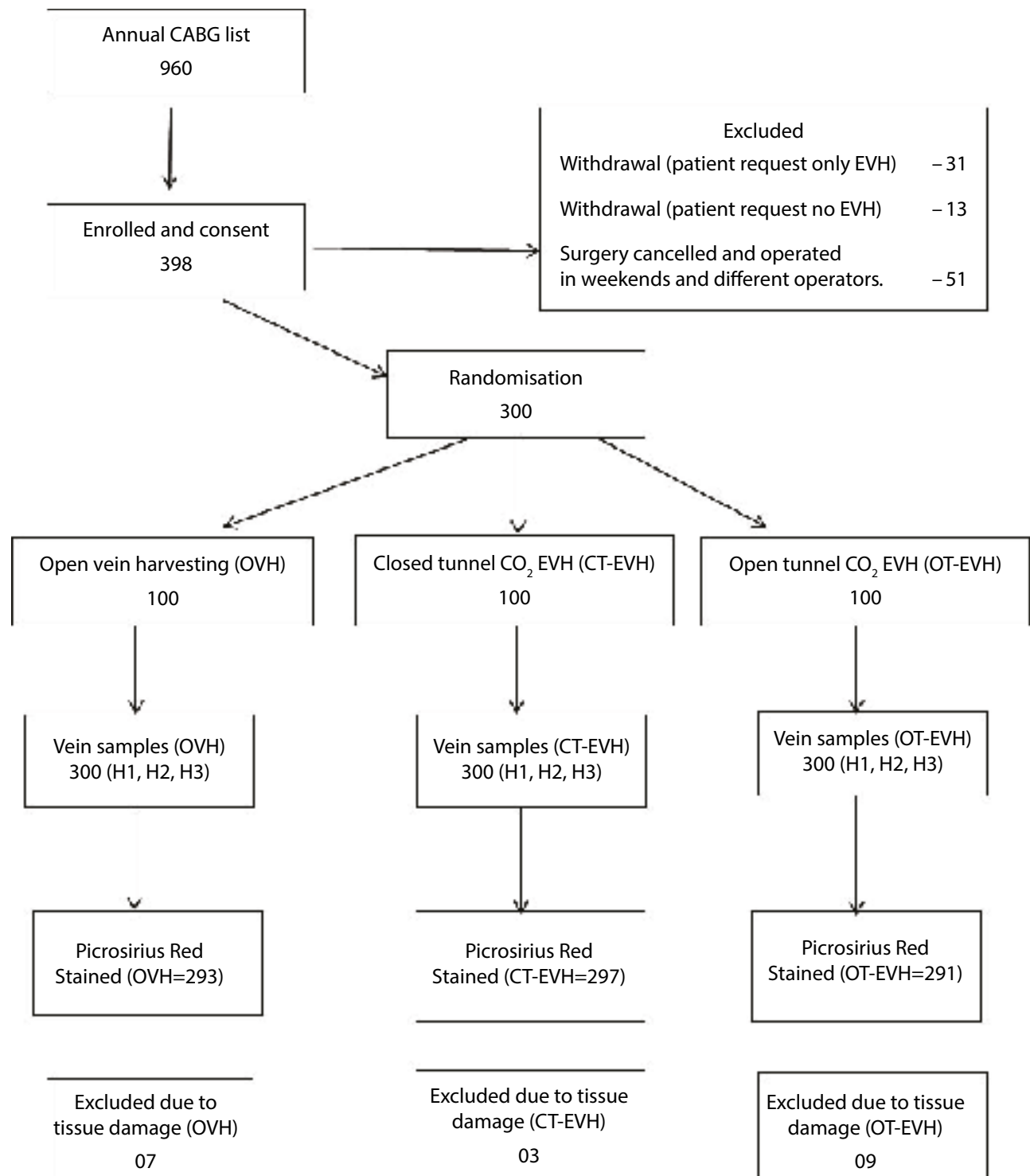


Figure 1 CONSORT flow diagram showing patient enrollment, histologic vein samples, and tissue damage. CABG, coronary artery bypass grafting; EVH, endoscopic vein harvesting

The CT-EVH procedure was performed using the Maquet VasoView HemoPro 2 system (Getinge). The carbon dioxide (CO₂) insufflation was maintained at a continuous flow rate of 3 L/min with a pressure of 10 mm Hg to establish a closed tunnel to facilitate vein dissection.

The OT-EVH procedure was performed using the Sorin ClearGlide (Sorin International) harvesting system. The CO₂ insufflation was set at a flow rate of 3 L/min with pressure maintained at 0 mm Hg, thereby avoiding the creation of a pressurized tunnel during conduit retrieval.

Sample Storage and Processing

Detailed methods for tissue processing and histologic scoring study protocol have been published previously as part of the main VICO trial article.⁵ The present study specifically used Picrosirius red staining to assess structural integrity of the vein wall. From each patient, 3 vein segments measuring approximately 1 cm were collected (H1, H2, and H3).

All samples were fixed in 4% formalin prepared in distilled water (pH 7.4). The H1 proximal segment was obtained immediately after harvesting and immersed in fixative before cannulation and flushing for leakage assessment. Subsequently, all veins were distended to a pressure of 20 mm Hg using VasoShield pressure-controlling syringe, after which the H3 distal segment was excised. The H2 segment was obtained at the end of the surgical procedure after completion of conduit manipulation and exposure to distension. Each specimen was assigned a numerical code to ensure blinding and transported in formalin to the research laboratory for histologic processing.

Histology Assessment

Picrosirius red staining

Picrosirius red staining was selected because it provides excellent visualization of collagen fibers and overall vessel wall architecture, facilitating assessment of structural integrity, including disruption of the intimal and medial layers and detachment of the longitudinal and circular smooth muscle layers, according to the predefined histologic scoring system. The stain was not used to assess cellular viability. Picrosirius red staining was performed to assess the structural integrity of the muscular and intimal layers. All specimens were processed according to a standardized protocol.¹⁹ Paraffin-embedded vein sections were deparaffinized and rehydrated in distilled water. Nuclei were stained for 8 minutes using Weigert hematoxylin A and B solutions, followed by rinsing in running tap water for 10 minutes. Sections were then incubated for 1 hour at room temperature in 0.1% (w/v) Direct Red 80 (picrosirius red; Sigma-Aldrich Ltd) prepared in a saturated aqueous solution of picric acid (Sigma-Aldrich Ltd). Slides were washed in 2 changes of acidified water, drained, and blotted dry. Rapid dehydration was performed using 2 to 3 changes of 100% ethanol followed by xylene, and coverslips were mounted using a resinous medium.

Histologic scoring

Longitudinal and circular smooth muscle layer integrity was evaluated using a validated scoring system with minor modifications.⁵ Muscular hypertrophy, detachment, and external and internal muscle migration were graded on a 4-point ordinal

scale (0–3), representing normal, mild, moderate, or severe changes. Disruption of the intima and medial connective tissue was quantified on a continuous scale from 0% (no disruption) to 100% (complete disruption).

Image acquisition and analysis

Picrosirius red- and hematoxylin-eosin-stained slides were digitally scanned using the Panoramic Viewer 250 (3DHISTECH) slide scanning system equipped with high numerical aperture Carl Zeiss optics (3DHISTECH), achieving a maximum image resolution of up to 0.16 μm per pixel. Digital images were viewed, annotated, and archived using Panoramic Viewer 250 platform. All scorers performed assessments within this software environment. Data were exported and analyzed using IBM SPSS Statistics, version 22 (IBM Corp) for analysis.

Statistical Analyses

The VICO trial⁵ primary end point was the extent of histologic tissue damage across 3 vein harvesting techniques. Sample size estimation was based on prior pilot histologic data, as no published studies were available to inform effect size assumptions.

A total of 91 patients per groups (CT-EVH, OT-EVH, and OVH), giving 273 patients overall, was calculated to provide 80% power to detect an absolute difference of at least 20% in the proportion of specimens demonstrating zero vein integrity (eg, 20% vs 40%). This calculation was based on a 2-group comparison using a simple χ^2 test with continuity correction at a 2-sided significance level of 5%. To allow for an anticipated 10% attrition rate, 300 patients were recruited.

All statistical analyses were performed using SPSS version 22 (IBM). Data distribution was formally assessed using the Shapiro-Wilk test. Normally distributed data are presented as mean (SD), whereas non-normally distributed data are expressed as median [IQR]. Categorical variables were analyzed using the χ^2 test. Continuous variables were analyzed using 1-way analysis of variance for parametric data or the Kruskal-Wallis test for nonparametric data as appropriate.

Results

Demographics

Baseline demographic variables were recorded for all 3 vein harvesting groups. Detailed preoperative characteristics are presented in Table 1. No conversions from endoscopic to OVH were performed. The CT-EVH group included a higher proportion of current smokers, a greater incidence of left main stem disease, and a higher median BMI compared

Table 1 An Overview of the Demographics of Each Group

Demographic variables	Groups		
	OT-EVH (<i>n</i> = 100)	OVH (<i>n</i> = 100)	CT-EVH (<i>n</i> = 100)
Age, y, mean (SD)	66.98 (10.06)	65.96 (9.27)	64.06 (10.20)
Sex, M/F, No. (%)	82/18 (82.0/18.0)	80/21 (79.2/20.8)	79/21 (79.0/21.0)
BMI, median [IQR]	27.77 [6.41]	28.08 [5.68]	28.95 [7.02]
Urgency, No. (%)			
Elective	46 (46.0)	50 (49.5)	41 (41.0)
Urgent	54 (54.0)	51 (50.5)	59 (59.0)
Diabetes, No. (%)			
Diet controlled	8 (8.0)	6 (5.9)	4 (4.0)
Tablet controlled	21 (21.0)	27 (26.7)	22 (22.0)
Insulin controlled	8 (8.0)	11 (10.9)	4 (4.0)
Canadian Cardiovascular Society, No. (%)			
I	17 (17.0)	18 (17.8)	12 (12.0)
II	25 (25.0)	29 (28.7)	33 (33.0)
III	45 (45.0)	45 (44.6)	46 (46.0)
IV	13 (13.0)	9 (8.9)	9 (9.0)
New York Heart Association, No. (%)			
I	27 (27.0)	32 (31.7)	40 (40.0)
II	45 (45.0)	36 (35.6)	26 (26.0)
III	26 (26.0)	25 (24.8)	29 (29.0)
IV	2 (2.0)	8 (7.9)	5 (5.0)
ST-elevated myocardial infarction, No. (%)	18 (18.0)	19 (18.8)	29 (29.0)
Non-ST-elevated myocardial infarction, No. (%)	42 (42.0)	48 (47.5)	44 (44.0)
Previous PTCA, No. (%)	16 (16.0)	12 (11.9)	20 (20.0)
Previous myocardial infarction, No. (%)	52 (52.0)	44 (43.6)	54 (54.0)
Multivessel disease, No. (%)	82 (82.0)	82 (81.2)	86 (86.0)
Left main stem, No. (%)	25 (25.0)	25 (24.8)	40 (40.0)
Hypertension, No. (%)	87 (87.0)	83 (82.2)	88 (88.0)
Smoking, No. (%)			
Never smoked	32 (32.0)	33 (32.7)	23 (23.0)
Previous smoker	52 (52.0)	55 (54.5)	47 (47.0)
Current smoker	16 (16.0)	13 (12.9)	30 (30.0)
Hypercholesterolemia, No. (%)	96 (96.0)	91 (90.1)	92 (92.0)
Peripheral vascular disease, No. (%)	19 (19.0)	20 (19.8)	21 (21.0)
Left ventricular ejection fraction, No. (%)			
>50%	74 (74.0)	75 (74.3)	71 (71.7)
30%–50%	21 (21.0)	18 (17.8)	22 (22.2)
<30%	5 (5.0)	8 (7.9)	6 (6.1)

Abbreviations: CT-EVH, closed-tunnel endoscopic vein harvesting; OT-EVH, open-tunnel endoscopic vein harvesting; OVH, open vein harvesting; PTCA, percutaneous transluminal coronary angioplasty.

with the other groups. Specimens were excluded due to tissue damage during harvest or processing and assessed by a blinded histopathologist. Excluded segments were distributed across all vein regions. However, the total number of analyzed segments remained balanced between groups ($n = 293$ OVH, $n = 297$ CT-EVH, and $n = 291$ OT-EVH).

Smooth Muscle Detachment

Circular muscle layer detachment

Across all sampling sites, the OVH technique demonstrated the highest proportion of normal circular muscle morphology (Figure 2), followed by CT-EVH and OT-EVH. Comparisons between techniques were performed across the 4 detachment categories (normal, mild, moderate, and severe) (Table 2).

At the proximal segment (H1), normal morphology was observed in 97 (99.0%) OVH samples compared with 81 (81.0%) CT-EVH and 79 (81.4%) OT-EVH samples. In the OVH group,

only 1 specimen (1.0%) demonstrated moderate detachment with no mild or severe changes. In contrast, CT-EVH demonstrated mild detachment in 13 (13.0%) samples, moderate detachment in 3 (3.0%), and severe detachment in 3 (3.0%). The OT-EVH group showed mild detachment in 12 (12.4%), moderate detachment in 4 (4.1%), and severe detachment in 2 (2.1%) samples. The distribution across the 4 detachment categories differed significantly between groups ($P = 0.008$).

At the random segment (H2), OVH again demonstrated the greatest structural preservation, with 97 (98.0%) samples classified as normal and only 2 (2.0%) showing mild detachment. In comparison, CT-EVH demonstrated normal morphology in 63 (63.6%) samples, with mild, moderate, and severe detachment observed in 22 (22.2%), 11 (11.1%), and 3 (3.0%) samples, respectively. The OT-EVH group demonstrated the lowest proportion of normal morphology (55 [56.1%]) and the highest degree of detachment, including mild detachment in 15 (15.3%), moderate detachment in 20 (20.4%), and severe detachment in 8 (8.2%) samples. The distribution of detachment grades differed significantly between techniques ($P < 0.001$).

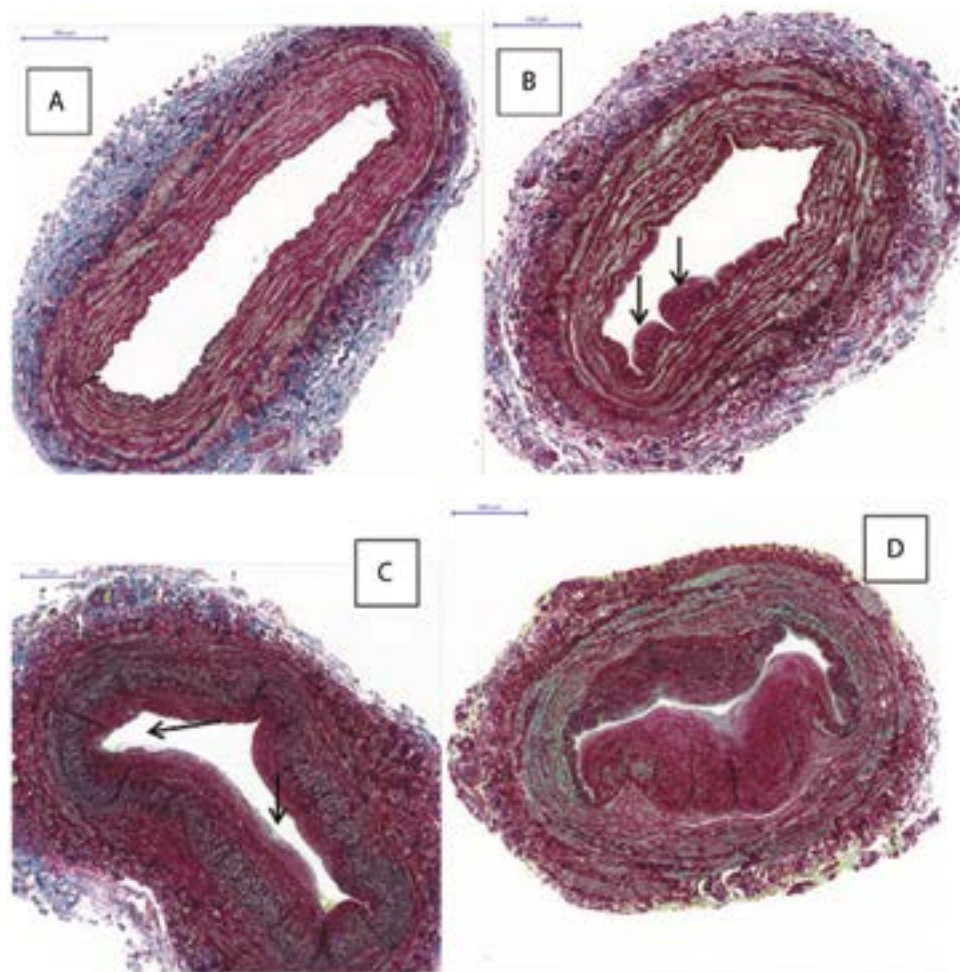


Figure 2 Cross-sectional long saphenous vein stained with picrosirius red (Scale bar = 500 μ m). A, Normal appearance of the vein. B, Black arrow indicates mild hypertrophy of the longitudinal muscle and muscle migration. C, Black arrow indicates intimal detachment and intimal stretching. D, Severe longitudinal hypertrophy almost occluding the vein

Table 2 Extent of Muscular Layer Detachment in Proximal, Distal, and Random Samples of the Long Saphenous Vein

Sample	Group	Normal	Mild	Moderate	Severe	<i>P</i> value
Circular layer detachment						
H1 (proximal)	OT-EVH	79 (81.4)	12 (12.4)	4 (4.1)	2 (2.1)	0.008
	OVH	97 (99.0)	0 (0.0)	1 (1.0)	0 (0.0)	
	CT-EVH	81 (81.0)	13 (13.0)	3 (3.0)	3 (3.0)	
H2 (random)	OT-EVH	55 (56.1)	15 (15.3)	20 (20.4)	8 (8.2)	<0.001
	OVH	97 (98.0)	2 (2.0)	0 (0.0)	0 (0.0)	
	CT-EVH	63 (63.6)	22 (22.2)	11 (11.1)	3 (3.0)	
H3 (distal)	OT-EVH	70 (72.9)	17 (17.7)	7 (7.3)	2 (2.1)	0.001
	OVH	95 (96.0)	4 (4.0)	0 (0.0)	0 (0.0)	
	CT-EVH	71 (72.7)	15 (15.2)	11 (11.1)	1 (1.0)	
Longitudinal layer detachment						
H1 (proximal)	OT-EVH	89 (91.8)	1 (1.0)	5 (5.2)	2 (2.1)	0.113
	OVH	95 (96.9)	3 (3.1)	0 (0.0)	0 (0.0)	
	CT-EVH	96 (96.0)	1 (1.0)	1 (1.0)	2 (2.0)	
H2 (random)	OT-EVH	93 (94.9)	0 (0.0)	4 (4.1)	1 (1.0)	0.380
	OVH	99 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	
	CT-EVH	89 (89.9)	5 (5.1)	3 (3.0)	2 (2.0)	
H3 (distal)	OT-EVH	88 (91.7)	2 (2.1)	1 (1.0)	5 (5.2)	0.012
	OVH	95 (96.0)	3 (3.0)	1 (1.0)	0 (0.0)	
	CT-EVH	91 (92.9)	1 (1.0)	2 (2.0)	4 (4.1)	

Abbreviations: CT-EVH, closed-tunnel endoscopic vein harvesting; OT-EVH, open-tunnel endoscopic vein harvesting; OVH, open vein harvesting. Values are No. (%).

At the distal segment (H3), normal morphology was present in 95 (96.0%) OVH samples compared with 71 (72.7%) CT-EVH and 70 (72.9%) OT-EVH samples. Mild detachment occurred in 4 (4.0%) OVH samples, whereas the CT-EVH group demonstrated mild, moderate, and severe detachment in 15 (15.2%), 11 (11.1%), and 1 (1.0%) samples, respectively. The OT-EVH group demonstrated mild detachment in 17 (17.7%), moderate detachment in 7 (7.3%), and severe detachment in 2 (2.1%) samples. The overall distribution across the 4 detachment categories differed significantly between groups ($P = 0.001$).

Longitudinal muscle layer detachment

It was generally uncommon across all techniques with OVH demonstrating the highest proportion of normal morphology followed by CT-EVH and OT-EVH in most segments. Comparisons were performed across the 4 detachment categories (normal, mild, moderate, and severe) (Table 2).

At the proximal segment (H1), normal morphology was observed in 95 (96.9%) OVH, 96 (96.0%) CT-EVH, and 89 (91.8%) OT-EVH samples. Mild detachment occurred in 3 (3.1%) OVH and 1 (1.0%) CT-EVH samples. Moderate detachment was

observed in 5 (5.2%) OT-EVH and 1 (1.0%) CT-EVH samples, whereas severe detachment occurred in 2 (2.1%) OT-EVH and 2 (2.0%) CT-EVH samples. The distribution across categories did not differ significantly between techniques ($P = 0.113$).

At the random segment (H2), all OVH samples demonstrated normal morphology (99 [100%]). In comparison, normal morphology was observed in 89 (89.9%) CT-EVH and 93 (94.9%) OT-EVH samples. Mild detachment occurred only in the CT-EVH group (5 [5.1%]). Moderate detachment was observed in 4 (4.1%) OT-EVH and 3 (3.0%) CT-EVH samples, whereas severe detachment was identified in 1 (1.0%) OT-EVH and 2 (2.0%) CT-EVH samples. The distribution across detachment categories was not significantly different between techniques ($P = 0.380$).

At the distal segment (H3), normal morphology was observed in 95 (96.0%) OVH samples compared with 91 (92.9%) CT-EVH and 88 (91.7%) OT-EVH samples. Mild detachment occurred in 3 (3.0%) OVH samples, 1 (1.0%) CT-EVH sample, and 2 (2.1%) OT-EVH samples. Moderate detachment was observed in 1 (1.0%) OVH, 2 (2.0%) CT-EVH, and 1 (1.0%) OT-EVH samples. Severe detachment occurred in 4 (4.1%) CT-EVH and 5 (5.2%) OT-EVH samples but was not observed in the OVH group. The distribution across the 4 detachment categories differed significantly between techniques ($P = 0.012$).

Smooth Muscle Migration

External muscle migration did not differ significantly between groups in H1 ($P = 0.121$), H2 ($P = 0.230$), or H3 ($P = 0.084$) samples. In contrast, internal muscle migration was significantly greater in OT-EVH across all sample types. In H1 samples, migration was observed in 86.6% of the OT-EVH group compared with 13.1% in OVH and 48.0% in CT-EVH ($P < 0.001$) (Figure 2).

A similar pattern was observed in H2 samples (43.9% in OT-EVH vs 11.0% in OVH and 29.3% in CT-EVH groups; $P < 0.001$) and H3 samples (OT-EVH [70.1%] vs OVH [7.0%] and CT-EVH [47.5%] groups; $P < 0.001$).

Intima and Medial Layer Disruption

Across all sampling sites, OVH consistently demonstrated the lowest levels of structural disruption, with median values of 0% for both intimal and medial layers. In contrast, both endoscopic techniques showed higher levels of disruption,

with CT-EVH generally demonstrating lower disruption than OT-EVH for the intimal layer, whereas medial disruption was comparable or slightly higher in CT-EVH than in OT-EVH.

For intimal disruption, the highest median levels were observed in the OT-EVH group across all segments (H1, H2, and H3), with values of approximately 6%, 11%, and 10%, respectively. The CT-EVH group demonstrated lower median intimal disruption, measuring approximately 4% at H1 and H3 and 4% to 5% at H2. No measurable intimal disruption was observed in the OVH group (all $P < 0.001$) (Figure 3).

For medial disruption, median levels were low across all techniques. In the OT-EVH group, median medial disruption was approximately 2% at H1, 3% to 3.5% at H2, and 2% at H3. The CT-EVH group demonstrated similar or slightly higher values, with approximately 2% at H1, 4% at H2, and 2.5% to 3% at H3, whereas the OVH group again demonstrated no detectable disruption (all $P < 0.001$) (Figure 3).

Intimal disruption in OT-EVH was most explicit in distended segments, suggesting that the combination of endoscopic harvesting and vein manipulation may contribute to increased intimal injury.

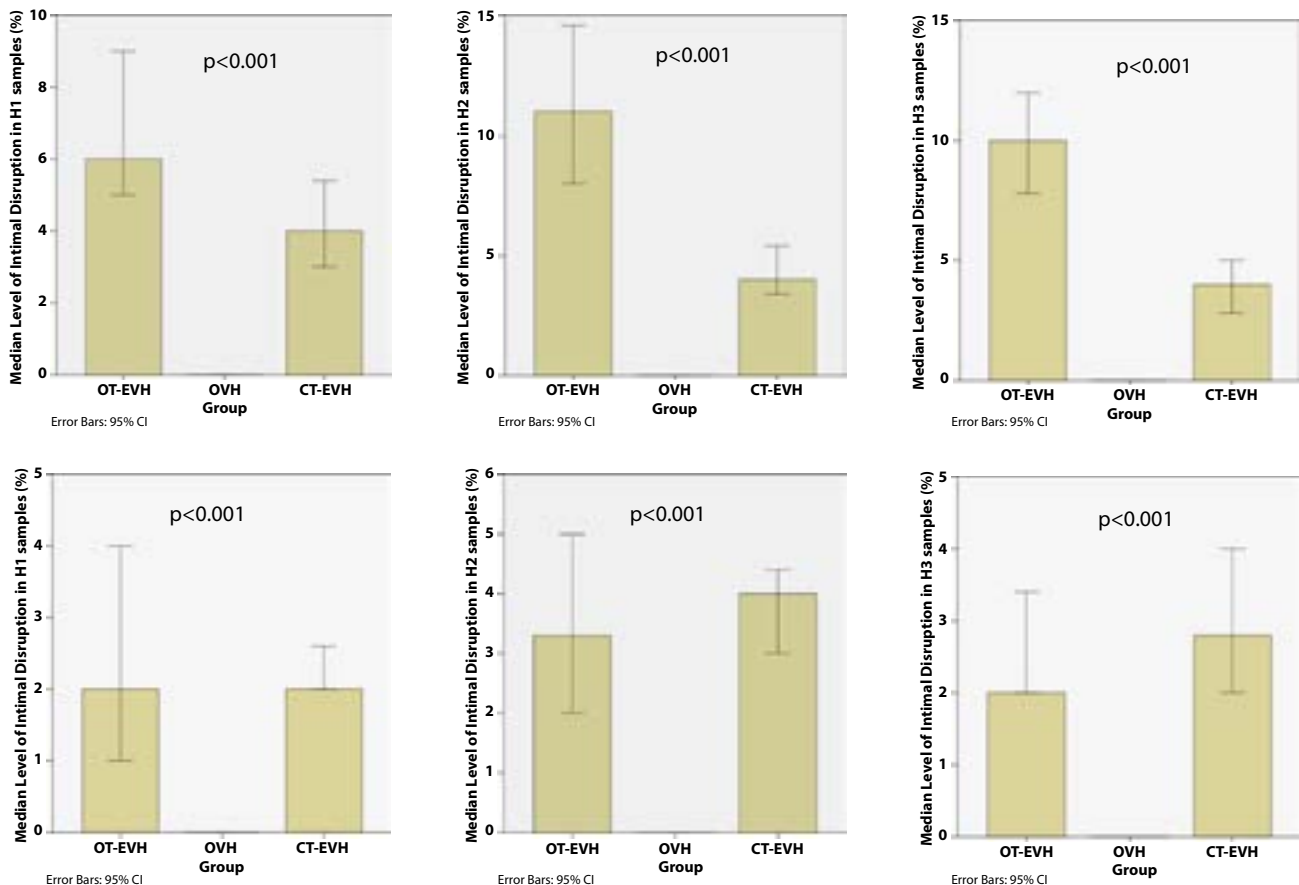


Figure 3 Median level of intimal and medial disruption in proximal, distal, and random vein samples. CT-EVH, closed tunnel endoscopic vein harvesting; OT-EVH, open tunnel endoscopic vein harvesting; OVH, open vein harvesting

Discussion

Many cardiac centers have adapted EVH technique as a standard practice following the 2017 International Society for Minimally Invasive Cardiothoracic Surgery (ISMICS) consensus statement, which classified wound morbidity reduction and patient satisfaction as class I, level A. Major adverse cardiac events (MACE) and noninferior patency rate outcomes at 1 to 5 years were assigned class III, level B-R.²⁰ However, previous studies did not examine the impact of vein distension, the learning curve, or histologic damage during harvesting, which led us to conduct this study.

Venous grafts exhibit higher rates of occlusion and failure than arterial grafts because of exposure to the high-pressure arterial system.¹⁴⁻¹⁸ Elevated arterial pressure promotes adhesion molecule expression, growth factor release, and extracellular protein deposition contributing to intimal thickening and smooth muscle proliferation.^{21,22} Consequently, evaluating the impact of harvesting technique on graft integrity is critical.

This study is the first to assess proximal, random, and distal vein samples to compare distended, minimally distended, and nondistended veins. Histologic analysis demonstrated structural changes dependent on the harvesting method. Proximal samples from OT-EVH more frequently exhibited mild intimal disruption, whereas severe intimal damage was uncommon, likely reflecting manual dissection performed near the vein. According to the literature, intimal disruption may predispose to thrombosis, medial disruption may lead to smooth muscle proliferation and intimal hyperplasia, and smooth muscle migration could contribute to luminal narrowing.²⁰⁻²⁵ Severe intimal disruption and elongation can constrict the vessel lumen and contribute to graft failure.²¹⁻²³

Random (H2) samples demonstrated the greatest degree of intimal disruption, particularly in the OT-EVH group, whereas CT-EVH showed lower levels of injury and OVH demonstrated no measurable disruption, indicating that harvesting-related manipulation may contribute to structural damage. Consistent with previous studies, cardioplegia, surgical manipulation, and distension can induce acute endothelial injury and cytoskeletal damage.^{21,24,25}

Smooth muscle hypertrophy, detachment, and migration appeared more pronounced in the circular layer than in the longitudinal layer and were more frequently observed in veins harvested using EVH techniques than in those harvested using OVH. These findings align with prior animal canine studies demonstrating that minimal mechanical manipulation preserves endothelial and medial integrity.^{26,27} Shear stress, radial and longitudinal deformation, and manual handling contribute to medial stretch, hypertrophy, and migration toward the lumen.^{8,28-30} Despite precautions to minimize trauma, histologic damage observed in OT-EVH may reflect the design of the equipment, which necessitates working close to the vein, potentially causing device-induced friction on the adventitia, smooth muscle, and endothelium.

Clinical Significance

A UK multicenter retrospective analysis of 27 024 patients over 10 years reported lower mortality with EVH than with OVH.⁴ However, adoption of EVH should be implemented with structured training and standardization of equipment, because practitioner experience influences outcomes.³¹⁻³³ Although clinical outcomes such as MACE were not directly assessed in this study, histologic preservation of vein structure may influence long-term graft patency. Our secondary clinical outcomes analysis from the main VICO trial revealed no significant differences in composite MACE events up to 48 months.⁵ However, routine angiographic or CT assessment of graft patency was not performed; therefore, direct correlations between the histopathologic changes observed in this study and long-term graft patency cannot be established. Future studies incorporating serial graft imaging alongside detailed histologic assessment would help determine the clinical significance of these structural alterations. Here, our findings emphasize the need for meticulous surgical technique and appropriate device selection to limit structural injury, which may ultimately influence graft durability.

Limitations

This study did not assess vasomotor function or gene expression changes, which are important to fully understand conduit viability. Functional assessment using transmission and scanning electron microscopy was also not performed. The greater integrity observed in OVH may reflect the operator's extensive experience (>2000 cases) compared with EVH (>250 cases per technique). Advanced and standardized training may mitigate the histologic impact of EVH. According to literature that EVH can be performed safely but careful patient selection and appropriate choice of EVH equipment remain essential.³⁴ Although all vein harvests were performed by practitioners who had completed at least 250 procedures with each harvesting technique, this study was not designed to assess the effect of increasing operator experience or learning curves on histologic outcomes. Consequently, we cannot determine whether further experience beyond this threshold would reduce the degree of structural injury observed with EVH. Routine postoperative graft imaging and assessment of graft-specific complications were not performed. Consequently, correlations between the histologic injury observed in this study and either early graft-related complications or long-term graft patency could not be evaluated.

Conclusion

OVH preserves saphenous vein structural integrity better than endoscopic techniques. Among EVH approaches,

OT-EVH was associated with the greatest intimal disruption across both nondistended and distended vein segments, with the most pronounced injury observed in manipulated or distended segments. In contrast, CT-EVH demonstrated greater medial layer disruption. These findings suggest that harvesting technique and device-related manipulation influence patterns of conduit injury. Meticulous technique and careful device handling may therefore be important to minimize structural damage. While EVH offers benefits in reducing wound morbidity, potential effects on conduit integrity should be considered when selecting harvesting devices and training practitioners.

Author Contributions

Sam Raaj: First draft writing and final review of the manuscript.

William R. Critchley: Data entry, data analysis, and final review of the manuscript.

Nehru Devan and Janesh Nair: Patient recruitment, data collection, and final review of the manuscript.

Muhammad Khawaja, Stuart Grant, and James B. Barnard: Final review of the manuscript.

Azita Rajai: Data analysis, interpretation, and final review of the manuscript.

Bhuvaneswari Krishnamoorthy: Conceptualization, design, methodology, data interpretation, supervision, and writing/review of the manuscript.

Conflict of Interest

The authors declare no conflict of interest.

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Ethics Approval

Ethical approval was obtained from the NRES Committee Northwest – Greater Manchester East, and all study participants provided written informed consent.

Data Availability

All coded data are available from the corresponding author and medical statistician on reasonable request.

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Ex Vivo Lung Perfusion in Lung Transplantation: Clinical Impact and Expanding Horizons

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Abstract

Ex vivo lung perfusion (EVLP) is an innovative technique in which the lungs are ventilated and perfused outside the human body. It helps simulate normal physiological conditions, provides additional time to assess normal lungs and recondition marginal lungs, extends lung preservation time, and serves as a platform for therapeutic interventions. The technique has evolved over the last couple of decades from simply assessing lungs before transplantation to a wide range of applications, including lung repair, reconditioning, and reengineering. This evolution has increased the number and quality of lung transplants, leading to improved overall transplant outcomes. After recovery from the donor, the lungs are connected to the EVLP machine, which establishes ventilation and perfusion. Subsequently, physiologic and biochemical parameters are assessed serially, along with imaging, to determine their suitability for transplantation. Issues such as atelectasis, pulmonary emboli, bacterial colonization with early signs of pneumonia, and pulmonary edema can now be effectively treated during EVLP, ensuring optimal use of lungs for transplant. Beyond treating marginal lungs, EVLP has other impressive applications for standard donor lungs, including immunomodulation, blood group conversion, gene therapy, virus inactivation, and tissue engineering. The primary goal of EVLP is to increase the donor lung pool while reducing morbidity and mortality on the transplant waitlist. With its growing use, EVLP has become a transformative technique, reshaping the landscape of lung transplantation and opening up potential for future applications in areas not yet imagined.

Keywords Ex vivo lung perfusion, lung transplantation, donor lung assessment

Background

Lung transplantation is the criterion standard procedure for patients with end-stage lung failure. However, the limiting factor is the availability of good-quality transplantable lungs. Currently, only about 20% of available lung donors are transplantable, which is substantially lower than the utilization rate for other solid organ transplants.¹ This is due to sequelae of brain death in the donor, leading to potential complications such as aspiration injury, traumatic injury, barotrauma injury due to the ventilator, or neurogenic pulmonary edema. Therefore, there is a strong rationale for maintaining the lungs under more

physiologic, normothermic conditions. Efforts have been made to expand the donor pool by using extended donor criteria and machine perfusion to salvage some rejected donor lungs.

Since the advent of lung transplantation, lungs have traditionally been flushed with a cold preservation solution during donor lung recovery and then stored on ice at approximately 4 °C (static cold storage). Cooling reduces metabolism, thereby decreasing the need for oxygen and nutrients. The main drawbacks of static cold storage are the inability to assess the suitability of lungs for transplantation after cold storage or to perform any therapeutic interventions and the abrupt transition from cold storage to reperfusion. Therefore, machine perfusion was developed to provide a platform for thorough evaluation before transplantation. The earliest use of machine perfusion dates back to 1935, when Carrel and Lindbergh² performed the first ex vivo organ perfusion, perfusing thyroid glands from cats and rabbits for up to 1 week. In the 1970s and 1980s, various attempts were made to implement ex vivo lung perfusion (EVLP) in different animal models, but it was not until the mid-1990s that Stig Steen revisited the clinical application of EVLP. The first successful EVLP was performed in 2001 using lungs from a donation after circulatory death (DCD) donor, which led to the first in-human

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lung transplantation after EVLP at the University of Lund in Sweden.³ This breakthrough paved the way for numerous clinical advancements that have transformed the landscape of lung transplantation.

Indications and Contraindications for EVLP

Common indications for EVLP include a Pao₂/Fio₂ ratio of 300 mm Hg or less, DCD lungs, concerning bronchoscopic findings, anticipated prolonged ischemic time, atelectasis, poor lung compliance, pulmonary edema, or pulmonary

embolism. The general contraindications include mechanical lung injury with air or blood leak, substantial contusions, active infectious disease, major aspiration, and malignancy.

The primary goals of EVLP are to increase the number of donor lungs available for transplant (Figure 1), to use it as a research tool, and to enhance the function and quality of otherwise marginal lungs (Figure 2).⁴ In clinical practice, EVLP has significantly expanded the donor pool, increasing overall lung transplant volumes by 15% to 20% at major transplant centers. For institutions regularly using EVLP, the technology successfully salvages and converts 50% to 70% of marginal or previously rejected donor lungs into viable organs for successful transplantation.⁴

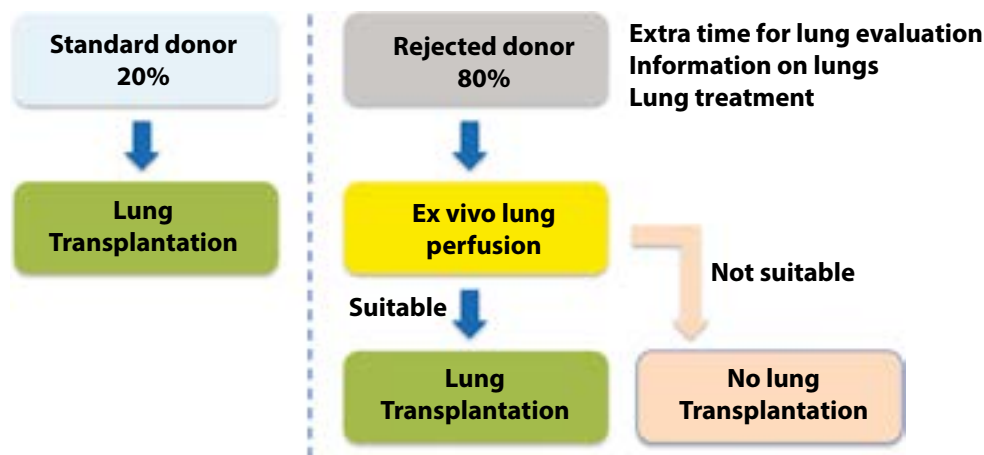


Figure 1 Ex vivo lung perfusion and lung transplantation

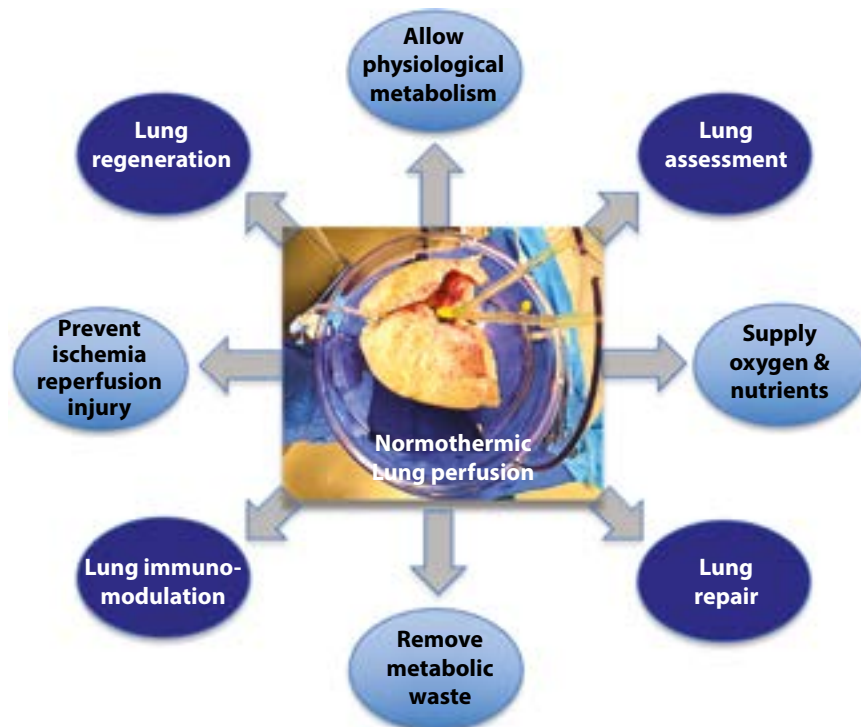


Figure 2 Benefits of ex vivo lung perfusion

The EVLP System

EVLP Protocols

Three protocols are used globally for EVLP—the Lund protocol, the Toronto protocol, and the Organ Care System (OCS) Protocol.⁵ The Lund protocol was originally developed in Sweden by Stig Steen and has undergone numerous modifications, culminating in the widely adopted Toronto Protocol. The third protocol involves the use of a portable EVLP machine that can be used at the donor site, causing a significant reduction in the cold ischemic time. Each protocol varies in its individual components, perfusate composition, flow rates, ventilator settings, and clinical application.

Currently, 2 major commercial EVLP devices are available in the United States—XVIVO Perfusion System (XPS) by XVIVO and OCS by TransMedics. In Canada, the TorEx Lung Perfusion System by Traferox is widely used and specifically designed for the Toronto Protocol, whereas in Europe, it is the Lung Assist by Organ Assist. Each device uses either 1 of the 3 standard protocols or a combination of them. The OCS by TransMedics is the only device used to transport lungs, whereas the other 3 are for in-house use.

EVLP Components

The EVLP system configuration is similar to that of a cardiopulmonary bypass circuit. Standard components include a centrifugal pump, a volume reservoir, a membrane oxygenator, a heat exchanger system, a leukocyte filter, a temperature probe, a flow sensor, perfusion solution, and an intensive care unit–type ventilator. These are enclosed in an integrated EVLP setup, with a separate sterile area for lung placement under a covered dome and a nonsterile area for perfusion circuit assembly (Figure 3A). The EVLP kit (Figure 3B) includes the reservoir, oxygenator, heater-cooler system, filter, proprietary cannulas for the left atrium (LA) and pulmonary artery (PA), a set of tubing, and a tri-gas cylinder (86% N₂, 8% CO₂, and 6% O₂). There are also 2 touchscreen interfaces—one for the surgeon and one for the perfusionist—that display real-time physiologic data of the lungs and the airway parameters. The most unique feature of the EVLP system is that it is configured to allow radiography of the lungs.

EVLP Methodology

The basic procedure of EVLP with the XPS system involves perfusion of the donor lungs via a closed system, with the perfusate being pumped antegrade into the PA cannula, returning via the LA cannula into the reservoir, which is further oxygenated by the membrane oxygenator and pumped back to the

PA by a centrifugal pump via a leukocyte filter. Typically, a perfusionist or EVLP specialist assembles the circuit before the lungs arrive, while a surgeon performs the surgical procedure on the lungs, oversees the lungs during the EVLP run, performs bronchoscopy at the end of every hour, assesses the suitability of the lungs for transplant based on the parameters, and discusses the findings with the implanting surgeon for a combined decision-making. The surgical part consists of suturing the LA and PA cannulas to their respective cuffs (Figure 3C), intubating the trachea with an endotracheal tube (Figure 3D), and securing it tightly to prevent dislodgement. The EVLP system works by delivering a solution of oxygen, proteins, and nutrients to injured donor lungs, allowing damaged cells to heal or preparing them for advanced repair methods. The perfusate used is STEEN Solution, a special mixture of human serum albumin, dextran, and an extracellular electrolyte composition. Reconditioning of the lung occurs through the removal of airway secretions, lung recruitment, resolution of pulmonary edema, washout of immunologic components, and activation of innate repair mechanisms within the lung.

After connecting the lungs to the EVLP circuit (Figure 3E), flow is initiated slowly in 10-minute increments, reaching the target peak flow of 40% of the estimated donor cardiac output by the end of 50 minutes. Lungs are slowly rewarmed to 37 °C, with ventilation initiated at 32 °C with a tidal volume of 7 mL/kg of ideal body weight, a respiratory rate of 7 breaths/minute, and a positive end-expiratory pressure (PEEP) of 5 cm H₂O. The tri-gas mixture used during ventilation simulates the normal physiologic environment, specifically to deoxygenate the perfusate and manage the partial pressure of carbon dioxide (pCO₂) within the perfusion circuit. The hypoxic gas mixture (low O₂) removes oxygen from the perfusate, mimicking the oxygen consumption of body tissues. There is a 10-minute recruitment phase at the end of every hour, with an increased ventilator setting to increase lung load, an oxygen challenge, and an inspiratory hold to a peak airway pressure of 20 cm H₂O. The various steps in EVLP are highlighted in Figure 3.

In the OCS protocol, the LA is open, ventilator settings are slightly different, and both perfusion and ventilation are initiated at 32 °C. The Lund protocol is similar, but with perfusion initiated at 15 °C and ventilation at 32 °C. Generally, EVLP can be performed for 4 to 6 hours using any of the protocols, although a decision to transplant the lungs can be made by the end of 3 hours of perfusion (Figure 3F). After the decision is made, the lungs are cooled to 15 °C at 50% FiO₂, and ventilation is terminated with the lungs half-inflated at 32 °C. The lungs are then stored in an ice cooler or in a 10 °C refrigerator (according to institutional protocol) until implantation. This is the start of the second cold ischemia time. Most centers aim for a second ischemic time of less than 4 hours to ensure optimal early graft function. However, large clinical databases from individual centers show that a second ischemic time exceeding 8 hours can still yield acceptable survival and mortality.⁶



Figure 3 Ex vivo lung perfusion (EVLP) assembly and steps. A, The integrated XPS EVLP system with the surgical, perfusion, and ventilator slots (Reproduced with permission from xvivogroup.com). B, EVLP circuit components: reservoir, centrifugal pump, oxygenator, leukocyte filter, and tubing set. C, Left atrial (LA) cannulation. D, Intubation of the lungs using a 9-mm endotracheal tube (ET tube) with double securing. E, Connection of lungs to the EVLP circuit. F, Well-inflated lungs during an EVLP run. G, Lung x-ray during EVLP with visualization of LA and pulmonary artery (PA) cannulas and ET tube.

Lung Assessment

The suitability of lungs for transplantation is determined using objective data on lung quality, including physiologic and biochemical parameters, as well as imaging techniques. At the end of each hour, perfusate samples from the LA and PA are sent for gas analysis to measure pO_2 , pCO_2 , pH, glucose, and lactate. The user interface displays real-time pulmonary vascular resistance, LA and PA pressures, airway pressure, plateau pressure, and dynamic compliance of the lungs. Bronchoscopy is performed either before or after the recruitment to clear secretions. Radiographic imaging is performed every hour to look for infiltrates in each lobe (Figure 3G). A deflation test and direct visualization of the lungs are performed to assess lung compliance and edema. Some centers also perform lung ultrasound and pulmonary angiography to quantitatively measure or treat pulmonary edema and pulmonary embolism.⁷

The comprehensive lung evaluation EVLP (COMPLETE) score used by the Cleveland Clinic is the composite result of 10 evaluation parameters, including lung weight measurement, ultrasound evaluation, airway pressure, compliance, oxygenation (P/F ratio or $\Delta pO_2 > 350$ mm Hg), lactate levels, bronchoscopy, radiography, and visual inspection (deflation, palpation). CLUE (Direct Lung Ultrasound Evaluation) is a specialized, patented technique used to measure lung water, which directly correlates with the likelihood of posttransplant

function.⁸ The criteria for lung acceptance after EVLP are outlined in the Table.

Discussion

The initial use of EVLP was limited to short runs for the DCD lungs to evaluate transplant suitability. However, with refinement in techniques and technologies, a more thorough evaluation of lung function using qualitative data has become possible. This has also made therapeutic interventions possible during EVLP for lung repair, reconditioning, and immunomodulation. The most common such intervention is adding a high-dose, broad-spectrum antibiotic to the perfusate during EVLP to treat a donor lung infection with early signs of pneumonia.⁹ Research published by Andreasson et al¹⁰ in 2014 demonstrated that adding broad-spectrum antimicrobial agents during normothermic perfusion leads to an absolute reduction in microbial load. Another study by Nakajima et al¹¹ in 2016 showed that human donor lungs rejected due to clinical infection, when treated with 12 hours of high-dose broad-spectrum antibiotic treatment during EVLP, had significantly reduced bronchoalveolar lavage bacterial counts and perfusate endotoxin levels.

Ischemia-reperfusion injury (IRI) is a major factor contributing to primary graft dysfunction (PGD) after lung transplantation. Various drugs, interleukin-10 gene therapy, and

Table Donor Lung Acceptance Criteria After Ex Vivo Lung Perfusion^a

Parameters	Criteria
Deflation	Complete: normal or near-normal rate
Compliance	<15% deterioration
Edema	No new or significant edema by imaging or palpation
Blood gases	Delta $pO_2 > 350$ mmHg or $PaO_2 > 350$ mmHg • Near consensus for delta $PaO_2 > 300$ mmHg
Overall movement	Acceptable • Poor movement in a few segments should be considered acceptable
STEEN Solution TM loss	Acceptable • >200 mL in the first hour is acceptable if it slows or stops by the next assessment
Bronchoscopy	Clear • Near consensus that nonrecurrent nonpurulent secretions are acceptable
Peak airway pressure	<15% increase
PVR	<15% increase
Weight gain	<15–20% increase
Causes for concern	• Severely abnormal or rapidly changing glucose or lactate • Diffuse abnormalities on imaging

Abbreviations: EVLP, ex vivo lung perfusion; PAP, peak airway pressure; PVR, pulmonary vascular resistance.

^aReproduced from Bacchetta et al. *J Thorac Dis.* 2025,⁴ which is licensed under a Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0) (<https://creativecommons.org/licenses/by-nc-nd/4.0/>).

cyclosporin A have been delivered to the lungs via the perfusate to mitigate IRI with encouraging results.^{12,13} Mesenchymal stem cells were successfully used by Lee et al¹⁴ to treat lung injury due to infection and endotoxins, as well as for an immunomodulatory role.¹⁵ Through the administration of exogenous surfactant immediately before EVLP, the lung parameters improved with a reduction in apoptotic cell death.¹⁶ Surfactant treatment and lung lavage also helped in aspiration injury to the lungs in a porcine experiment by Nakajima et al.¹⁷ Pulmonary embolism, which commonly occurs in donor lungs, can be successfully thrombolized using tissue plasminogen activator during EVLP.¹⁸ In an attempt to reduce the incidence of rejection, recipient-derived regulatory T cells were administered during EVLP, which led to inhibition of the conventional T-cell response in the immediate posttransplant phase, thus reducing posttransplant alloimmunity and subsequent infectious complications with augmented immunosuppression.¹⁹ Targeted RNA therapies have been used to immunomodulate donor lungs.²⁰ This method seeks to minimize recognition and sensitization by the recipient's immune system, while possibly enhancing markers of tolerance. Consequently, this could reduce both acute and chronic rejection rates, potentially lowering the requirement for long-term immunosuppression. Preclinical studies by Cypel et al²¹ exposed HCV+ blood to ultraviolet-C radiation during EVLP and demonstrated a reduction in HCV infectivity. Donor lungs treated with immunotoxins to treat latent human cytomegalovirus (CMV) showed a reduction in reactivation of CMV.²² In another groundbreaking study, ex vivo enzymatic treatment converted blood type A donor lungs into universal blood type lungs.⁵

EVLP is well suited to integrating artificial intelligence (AI), as the assessment of donor lungs is subjective and still lacks well-defined criteria. Moreover, large amounts of data can be obtained from serial hourly measurements of parameters during EVLP runs, and the data are isolated to the lungs, with no cross-signal from other organ systems. Sage et al.²³ from Toronto developed a machine-learning model named InsignTx, to aid surgical decision-making and predict posttransplant outcomes, using clinical EVLP data collected over a decade. A donor-recipient model was created that can evaluate donor lungs broadly for any recipient or be tailored with specific recipient details to personalize predictions for individual patients.

The short-, mid-, and long-term survival of patients transplanted with EVLP lungs is excellent across all studies.²⁴ The graft function in the immediate transplant period and long-term has been similar to that of patients transplanted with lungs not subjected to EVLP. The incidence of PGD and chronic lung allograft dysfunction-free survival was noninferior to transplantation with non-EVLP lungs, indicating that EVLP is not a risk factor.

Recent reviews of national transplant databases, such as the UNOS (United Network for Organ Sharing) registry, indicate

that recipients of EVLP-managed lung allografts experience similar or occasionally slightly higher rates of early postoperative extracorporeal membrane oxygenation (ECMO) use compared with standard cold-storage lungs.²⁵ This is because EVLP is used to evaluate and recondition high-risk donor lungs that would otherwise be turned down. Using these extended-criteria organs inherently carries a complex posttransplant recovery profile. A venovenous ECMO can be very useful in helping these marginal lungs recover in the immediate postoperative phase. The posttransplant ECMO use also varies based on DBD (donation after brain death) or DCD lungs.

A retrospective study by Peel et al²⁶ in 2023 tracked acute outcomes before and after EVLP introduction. Rather than long-term metrics, it specifically identified that the availability of EVLP correlated with shorter postoperative mechanical ventilation time, lower immediate likelihood of tracheostomy insertion, and decreased in-hospital mortality. Another study, a retrospective analysis focusing on short-term indices, analyzed US registry data, published by Jawitz et al.²⁵ Adjusting exclusively for acute indicators, the study showed that EVLP-perfused allografts demonstrated no significant difference in 30-day or 180-day recipient survival and matching rates of acute rejection before discharge compared with conventional transplants.

Future Implications

With the widespread clinical use of EVLP, EVLP as a research tool has vast opportunities. Extended multiday lung preservation and regeneration of new lungs hold more promise than ever.

The concept of multiday EVLP has been explored by many groups. The Toronto team was the first to successfully establish 3-day EVLP using a thoughtful combination of cold storage at 10 °C and intermittent EVLP cycles, with excellent posttransplant lung function.²⁷ A significant finding was that metabolites lost during cold storage were regenerated by EVLP, which also helped reduce mitochondrial injury. Other groups evaluated the feasibility of extended preservation with EVLP by using a variety of modalities, including perfusate adsorption/filtration techniques and the addition of plasma and/or donor whole blood to the perfusate, along with nutrients, vitamins, and amino acids. The use of pulsatility, low flows, hypothermia, positive outflow pressures, personalized ventilation settings tailored to the lung issue, and negative-pressure ventilation has been explored with interesting results.²⁸ More research is required to translate these experimental techniques to clinical applications. Extending lung preservation times to multiple days can have positive effects on transplant logistics, organ banking, and immunomodulation, enabling better donor-recipient matching.

Another promising approach under investigation is lung bioengineering using an EVLP scaffold, which provides a platform for regenerating new lungs.²⁹ New lungs can be created using whole-lung extracellular matrix scaffolds produced by perfusing cadaveric organs with decellularizing agents. The EVLP technique functions as a bioreactor, using vascular perfusion and liquid ventilation to repopulate the native lung matrix with endothelial and epithelial cells. This process ensures that cells are added in sufficient numbers and in their correct anatomical locations, which are essential for optimal organ function. This is a new field of study, and although we are far off from creating a fully functional bioengineered lung, ex vivo engineered lung tissues with effective oxygenation may be feasible. EVLP is a transformative technology with endless possibilities and future applications for evaluating organ responses to ischemia, quantifying inflammation, predicting reperfusion injury and alloimmune responses, and 3-dimensional printing of lung scaffolds.³⁰

Barriers to Implementation

Despite the substantial benefits of EVLP, the main barrier to its widespread use is the high cost—covering the system, personnel, and space. To address this, centralized EVLP centers are becoming more common and viable, and some centers are developing custom EVLP systems that are less expensive and tailored to their needs.

Conclusion

EVLP has become a key adjunct to lung transplantation over the years and continues to evolve. The technology has evolved from early experiments into a strong clinical tool that overcomes the restrictions of traditional donor lung evaluation. Implementing EVLP offers a promising approach to use marginal donors by reducing IRI and aiding the repair and regeneration of suboptimal grafts. EVLP significantly broadens the donor pool, increases transplant volumes, reduces waitlist morbidity and mortality, improves tolerability of cold ischemia time, and enhances overall graft function after transplantation. With further advances in biomolecular techniques for repairing damaged donor lungs or regenerating new ones, this platform has the potential to enable organ modification, thereby advancing medical science and bioengineering. The incorporation of advanced perfusion solutions and AI-powered assessments offers significant promise for the future of EVLP. With growing use, EVLP has become a transformative technique, reshaping the landscape of lung transplantation and paving the way for future applications yet to be imagined.

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Current Trends in Coronary Artery Bypass Grafting: Innovations Shaping Modern Coronary Revascularization

M. Arockia Grazy

Introduction

Coronary artery disease (CAD) remains the most common form of heart disease encountered worldwide. CAD that manifests as myocardial infarction (MI), or heart attack, in its severe form is one of the leading causes of global mortality.¹

Coronary artery bypass grafting (CABG) remains the gold standard for the treatment of complex multivessel CAD despite remarkable advances in percutaneous coronary intervention (PCI). Although percutaneous interventions have transformed the management of CAD, CABG continues to provide superior long-term outcomes in selected patients.² Over the past 2 decades, continuous innovations in surgical techniques, conduit selection, perioperative care, and digital technologies have transformed CABG into a safer, less invasive, and increasingly personalized procedure. This review summarizes the major contemporary trends shaping modern coronary revascularization.

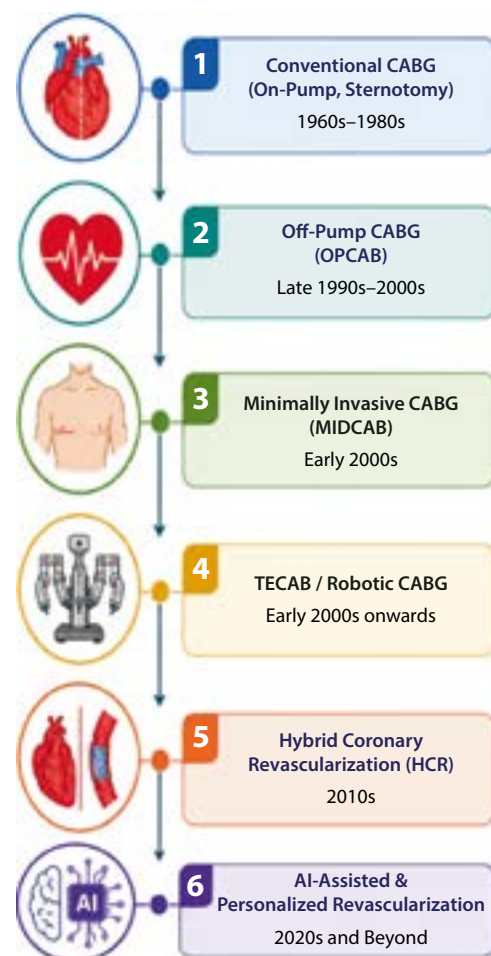
History of CABG

The concept of CABG was developed to bypass blocked coronary arteries and establish blood flow beyond the occluded portion of the artery. Over the years, CABG has evolved into a lifesaving procedure for patients with complex multivessel CAD.³ Some historical landmark events in the development of CABG are implantation of the left internal thoracic artery (LITA) directly into the free wall of the left ventricle by Dr Arthur Vineberg in 1946 and the first successful anastomosis of the right internal thoracic artery to the right coronary artery (RCA) by Dr Robert Goetz in 1960.

The use of the LITA to the left anterior descending coronary artery (LAD) by Dr George Green in 1968, followed by the introduction of the radial artery as a conduit by Dr Alain Carpentier in 1972, established the foundation for modern

Evolution of Contemporary Coronary Artery Bypass Grafting

From conventional surgery to personalized, technology-driven revascularization



CABG: Coronary Artery Bypass Grafting; OPCAB: off-Pump CABG;
MIDCAB: Minimally Invasive Direct CABG; TECAB: Totally Endoscopic CABG;
HCR: Hybrid Coronary Revascularization; AI: Artificial Intelligence.

arterial revascularization. The 1990s witnessed the introduction of minimally invasive direct coronary artery bypass (MIDCAB), and in 1998, Dr Didier Loulmet performed the first totally endoscopic coronary artery bypass (TECAB) surgery. Present-day robotic coronary surgery has developed by integrating these techniques.

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Major Impact Trials in Cardiac Surgery

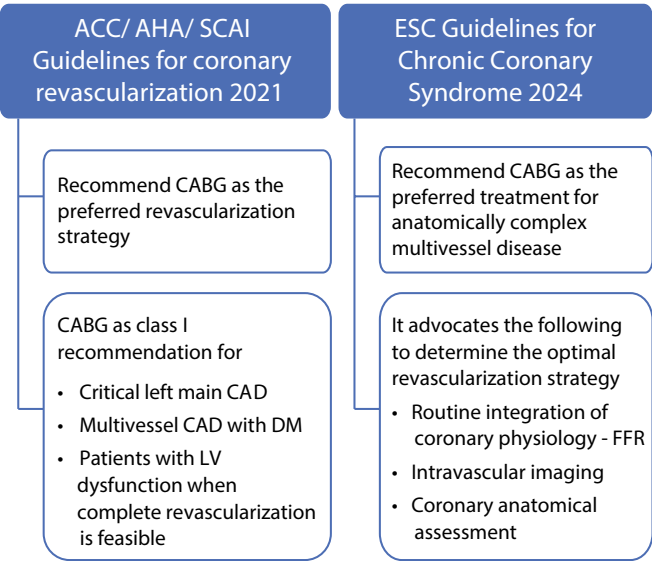
The below table illustrates the major trials in cardiac surgery that have shaped modern revascularization and surgical techniques, transforming historical observations into evidence-based practices.⁷⁻²⁰

Trial	Year	Study sample	Main finding	Clinical impact
<i>CABG VS MEDICAL THERAPY</i>				
BARI	1996	Multivessel CAD	CABG superior in diabetics	Established diabetic benefit
STICH	2011	EF < 35%	CABG improved survival	Landmark heart failure trial
STICHES	2016	10-y follow-up	Sustained mortality benefit	CABG standard in ischemic cardiomyopathy
<i>CABG VS PERCUTANEOUS INTERVENTIONS</i>				
SYNTAX	2009	Left main stenosis with multivessel disease	CABG reduced repeat revascularization and MACE	Introduced SYNTAX score
SYNTAXS	2019	10-y follow-up	Survival benefit in complex CAD	Reinforced CABG
FREEDOM	2012	DM + multivessel disease	Lower mortality and MI after CABG	CABG as class I recommendation
EXCEL	2019	Left main disease	Comparable early outcomes; controversy over long-term mortality	Help refine anatomical complexity scores and guidelines
NOBLE	2020	Left main disease	CABG with superior long-term results	Favored CABG
FAME 3	2021	3 vessel diseases	PCI failed noninferiority	Reinforced CABG as the standard strategy
<i>OFF-PUMP CORONARY ARTERY BYPASS GRAFTING (OPCAB) VS ON-PUMP</i>				
CORONARY	2016	OPCAB vs on-pump	Similar long-term outcomes	Both acceptable
ROOBY	2016	OPCAB vs on-pump	Slightly higher repeat revascularization in OPCAB	Importance of surgeon's experience
<i>GRAFT SELECTION IN CABG</i>				
ART	2019	Single vs bilateral internal thoracic artery (ITA)	Similar 10-y survival	Debate on multiarterial grafting
ROMA	Ongoing	Single vs multiple arterial grafts	Awaiting definitive survival data	May redefine conduit strategy

Abbreviations: ACC, American College of Cardiology; AHA, American Heart Association; SCAI, Society for Cardiovascular Angiography and Interventions; DM, diabetes mellitus; LV, left ventricular; ESC, European Society of Cardiology; FFR, fractional flow reserve

Over the past 3 decades, advances in surgical technology, conduit selection, perioperative care, and hybrid revascularization strategies have substantially transformed CABG. The following sections summarize the most important contemporary developments.

Contemporary Guideline Recommendation for Coronary Revascularization⁴⁻⁶



Current Trends in CABG

a. Minimally Invasive Cardiac Surgery

The development of PCIs and modern-day advancements in surgical techniques have enabled surgeons to perform

minimally invasive coronary surgery, even in a multivessel setting.

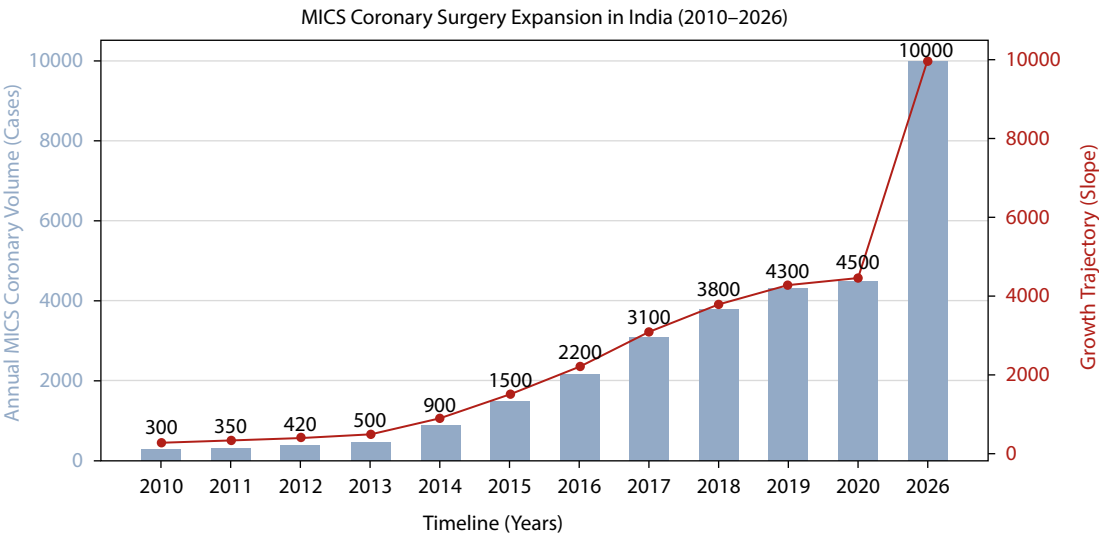
- i. MIDCAB, where the ITA harvesting and coronary anastomosis are performed through an anterior minithoracotomy to avoid sternotomy and its complications.
- ii. TECAB, where the ITA harvesting and coronary anastomosis are performed through an endoscope in a closed chest.
- iii. Robotic coronary surgery combines both techniques, wherein the ITA is harvested using an endoscope and the anastomosis is performed via minithoracotomy. At present, the da Vinci robotic system (Intuitive Surgical, USA) is the only available system.

The advantages of minimally invasive cardiac surgery (MICS) over the conventional CABG are as follows:

- Reduction of the superficial and deep sternal wound infections and mediastinitis.
- MIDCAB allows the feasibility of harvesting bilateral ITAs without compromising the sternal healing, as in the case of sternotomy. The long-term patency of the ITA is preserved, which stands as the gold standard in treating LAD lesions, even when the vessel is diffusely diseased, calcific, ectatic, and tortuous in nature.²¹
- Faster postoperative recovery that results from shorter intensive care unit and hospital stays.
- Reduced incidence of postoperative stroke due to less manipulation of the aorta.²²
- The cosmetic outcome is obvious from the patient’s point of view.

The drawbacks of minimally invasive coronary surgery are as follows:

- Feasibility of the MIDCAB in patients with morbid obesity comes with technical challenges, especially with the need of



peripheral cannulation to establish cardiopulmonary bypass (CPB) to avoid sternotomy.

- The learning curve could be steeper for surgeons, especially with robotic CABGs.
- It demands longer operating time during the initial period and involves substantial costs.

With proper patient selection and planning, minimally invasive coronary surgery serves as a safe and effective alternative to more invasive conventional CABGs.²³

b. Off-Pump Coronary Artery Bypass Grafting

The emergence of off-pump coronary surgery, which avoids the use of the CPB machine and its complications, made a significant impact on the evolution of CABG, directing the development and growth of the minimally invasive procedures that followed.

OPCAB was developed to decrease perioperative complications associated with traditional on-pump surgery. It aims to reduce complications of CPB, such as perioperative myocardial injury, stroke, and renal failure, and improve long-term outcomes. However, trials from across the globe demonstrates no significant difference between on-pump and off-pump CABGs in terms of morbidity, mortality, and the need for subsequent reinterventions.²⁴

c. Total Arterial Coronary Revascularization

Beyond refinements in the surgical approach, contemporary CABG has also evolved through improvements in conduit selection. Total arterial coronary revascularization (TAR) has gained supremacy over the use of saphenous vein as a traditional venous conduit of choice for CABG. Accelerated atherosclerosis and inferior patient outcomes associated with venous grafts have led the surgeons to favor arterial conduits, particularly bilateral internal mammary arteries and the radial artery.

Some benefits and limitations of TAR are as follows²⁵:

Benefits	Limitations
• Long-term patency rates • Graft longevity • Decreased rate of repeat revascularization • Prevention of major adverse cardiac events like MI or death	• Technically challenging • Sternal wound infection • Delayed healing (bilateral ITA) • Comparatively longer operating time

- Skeletonized ITA may offer advantages, including extra length, reduced chest wall complications, and lesser chest wall pain.
- Fractional flow reserve–guided CABG is gaining importance as a tool to guide the indications for arterial grafts and may thereby improve clinical outcomes.

Conduit	10-y patency	Advantages	Limitations	Guideline position
Left internal thoracic artery	90%–95%	Excellent long-term survival; resistant to atherosclerosis	Single conduit	Gold standard (class I)
Right internal thoracic artery	85%–90%	Excellent durability	Increased sternal wound risk in selected patients	Recommended in selected patients
Radial artery	80%–90%	Better than saphenous vein graft; good long-term patency	Vasospasm; requires severe target stenosis	Preferred second conduit
Saphenous vein	50%–60%	Easy harvest; long length	Intimal hyperplasia; atherosclerosis	Widely used
Gastroepiploic artery	65%–75%	Useful for RCA territory	Technical complexity	Selected cases

d. Anaortic CABG

One of the most important contemporary developments is anaortic CABG, also known as the no-touch aorta technique. Modern coronary surgery increasingly focuses on avoiding manipulation of the ascending aorta, which represents the principal source of cerebral embolization during CABG.

The anaortic technique eliminates cross/side clamping of the aorta and proximal anastomosis using the following:

- Bilateral internal thoracic arteries
- Composite Y grafts
- Sequential arterial grafting
- In situ arterial inflow

e. Epiaortic Ultrasound

Epiaortic ultrasound is an important tool used to assess the ascending aorta and thereby modify the operative strategy to prevent embolization. Epiaortic ultrasound provides real-time visualization of the following:

- Calcific plaques
- Mobile atheroma
- Intimal thickening
- Safe cannulation sites

f. Transit-Time Flow Measurement

Transit-time flow measurement (TTFM) is widely used to assess graft function before chest closure to ensure intraoperative graft quality.

TTFM measures	TTFM identifies	Uses of TTFM
Graft flow	Graft kinking	Improves graft patency
Pulsatility index	Anastomotic narrowing	Reduces the risk of early graft failure
Diastolic filling	Competitive flow	

g. Hybrid Coronary Revascularization

Hybrid coronary revascularization (HCR) procedure is a combination of MIDCAB, which offers LITA to the LAD as an off-pump beating-heart procedure, and PCI to treat coronary arteries other than the LAD. This technique is useful in case of a multivessel CAD, where the benefits of the ITA are retained.²⁶

HCR provides the benefits of MIDCAB and PCI, which include faster recovery, lower blood transfusion rates, and reduced hospital stay. There are convincing evidences available to demonstrate the early- and midterm outcomes of HCR, while more long-term studies are needed to witness encouraging results over the conventional procedures.²⁷

h. Endoscopic Vein Harvesting

Endoscopic vein harvesting (EVH) has become the preferred choice and standard of care over traditional open vein harvesting (OVH) methods. EVH has evolved over the last 2 decades, demonstrating significant benefits over OVH in terms of reduced leg wound complications and surgical site infections.²⁸

Although the technique with experience has shown promising short-term benefits, with increasing surgical experience mid- and long-term evidence is required to establish graft patency and durability.

Additional emerging advances in coronary revascularization include the following:

i. Artificial Intelligence in Cardiac Revascularization

- Artificial intelligence (AI) is used in coronary surgery mainly to predict the postoperative complications and enhance decision-making with better preoperative risk assessment, stratification, and prognostication.²⁹
- Development of a fully-automated, AI-powered platform converts routine computed tomography (CT) coronary angiography into a patient-specific CABG planning platform using
 - Anatomical characterization
 - Automated target-site analysis
 - Virtual graft construction
 - Reduced order hemodynamic assessment.³⁰
- AI can play a vital role in improving the postoperative rehabilitation after CABG, by providing precise and tailored monitoring and treatment plans, and enabling better communication and risk prediction.³¹
- AI models need huge datasets, which lack heterogeneity and hence can be biased. Other limitations include lack of real-world authentication, regulatory uncertainty, and poor workflow integration.³²

ii. Three-Dimensional Imaging and Surgical Planning

Modern coronary CT angiography now extends beyond diagnosis. Three-dimensional reconstruction enables

- Coronary mapping
- Conduit planning
- Target vessel selection
- Simulation of graft configuration
- Assessment of calcification

AI is increasingly being integrated into these planning systems, allowing patient-specific operative strategies before entering the operating room.³³

iii. Gene Therapy, Stem Cell Therapy, Nanotechnology, and Augmented and Mixed Reality³³

	Gene therapy	Stem cell therapy	Nanotechnology	Augmented and mixed reality
Focus	Graft durability	Ischemic cardiomyopathy	Refine coronary surgery	Incorporate digital information
Mode	- Enhancement of endothelial nitric oxide production - Suppression of smooth muscle proliferation - Prevention of intimal hyperplasia - Promotion of angiogenesis - Reduction of inflammatory signaling	- Neovascularization - Paracrine signaling - Myocardial regeneration - Reduction of fibrosis	- Drug-eluting vascular grafts - Targeted anti-inflammatory therapy - Localized antiproliferative drug delivery - Advanced biosensors - Infection-resistant biomaterials	- Three-dimensional coronary visualization - Target vessel localization - Navigation of intramyocardial arteries - Composite graft planning - Surgical education
Reality	Still investigational	More clinical evidence needed	In early stages of research	Valuable in MICS and robotic surgery

Preoperative Optimization	Intraoperative Strategy	Postoperative Care
• Smoking cessation • Nutritional assessment • Diabetes optimization • Anaemia correction • Patient education • Frailty assessment • Carbohydrate loading where appropriate	• Goal-directed fluid therapy • Normothermia • Blood conservation • Multimodal analgesia • Reduced opioid exposure • Lung-protective ventilation	• Early extubation • Early oral feeding • Early mobilization • Delirium prevention • Physiotherapy • Glycemic control • Standardized discharge planning

iv. Enhanced Recovery After Cardiac Surgery

Enhanced recovery after cardiac surgery is an evidence-based multidisciplinary approach that is structured throughout the perioperative course and focuses on rapid rehabilitation, optimized pain control, early mobilization, and faster recovery.³⁴

Summary

Current trends	Advantages	Limitations
MIDCAB	Smaller incision, faster recovery	Learning curve
TECAB and robotics	Higher precision	Higher cost
OPCAB	Reduced CPB complications	Similar results to on-pump surgery
TAR	Superior long-term graft patency	Technically demanding, competitive flow, and vasospasm
HCR	Faster recovery	Needs long-term studies
EVH	Lower leg wound complications	Learning curve; vein trauma
AI	Enhanced procedural planning	Possibility of bias; needs data on clinical outcomes

In addition to the surgical advancements, the holistic approach to a patient undergoing cardiac surgery has gained more value in recent years.

Heart Team Approach

The management of CAD has moved into an integrated and collaborative heart team approach. Teamwork rather than an isolated specialty is essential in producing optimal decision-making strategies involving cardiac surgeons, interventional cardiologists, cardiac imaging specialists, heart failure physicians, and anesthesiologists.

Precision Revascularization

Modern coronary surgery has entered the era of precision revascularization, where treatment decisions are individualized using multiple complementary tools, including the following:

- Coronary CT angiography
- SYNTAX score II
- Fractional flow reserve
- Intravascular ultrasound
- Optical coherence tomography
- Myocardial viability imaging
- AI-assisted risk prediction
- Frailty assessment
- Shared decision-making

Current Challenges

Despite the robust advancements made in coronary revascularization, challenges remain evident and are listed below:

Parameter	Primary challenge	Clinical strategy and requirements
Ageing population	Balancing operative risk against long-term survival	Careful patient selection and risk stratification
Diabetes	Managing diffuse coronary disease	Optimizing conduit selection and ensuring proper wound healing
Frailty	Serving as an independent predictor of postoperative mortality	Implementing routine frailty assessments
Chronic kidney disease	Presenting an inherently high risk of complications	Investigating arterial grafting and renal protection strategies
Redo CABG	Executing technically demanding procedures	Requiring advanced surgical expertise and meticulous entry
Cost	Increasing overall health-care expenditure	Evaluating cost-effectiveness alongside clinical outcomes

The objective is no longer simply to restore coronary blood flow but to maximize long-term survival, preserve ventricular function, minimize repeat interventions, and optimize patient-reported outcomes.

Conclusion

Off-pump surgeries, hybrid procedures, graft selection, and procurement techniques have redefined the coronary revascularization and provide a tailored treatment option.³⁵

As technological innovation continues to converge with evidence-based surgical practice, the future of CABG lies in increasingly personalized, minimally invasive, and data-driven revascularization strategies while maintaining excellent long-term outcomes. Despite these advances, meticulous surgical technique, appropriate patient selection, and durable arterial grafting will remain the cornerstones of successful coronary revascularization.

Contemporary CABG is therefore no longer defined simply by the number of grafts performed but by the quality, durability, and biological suitability of each conduit. The future of coronary surgery lies in individualized conduit strategies that maximize long-term patency while minimizing operative risk.

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Sprays, Injections, and Topical Therapy: Are Vaccines on the Horizon for the Treatment of Recurrent Urinary Tract Infections in the United Kingdom?

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Abstract

Importance: Recurrent urinary tract infection (rUTI) is a common and burdensome condition, particularly in women, and generates substantial clinical workload across primary care, acute medicine, and urology. Prevention in UK practice has traditionally centered on behavioral measures, vaginal estrogen in peri- and postmenopausal women, nonantibiotic options such as methenamine hippurate, and, where needed, antibiotic prophylaxis. However, concerns about antimicrobial resistance, adverse effects, and microbiome disruption have increased interest in antibiotic-sparing approaches. This article reviews the emerging role of vaccines and vaccine-adjacent immunoprophylaxis for recurrent uncomplicated urinary tract infection (UTI), while distinguishing this pathway from catheter-associated UTI, complicated UTI, and urosepsis.

Observations: Current evidence suggests that the sublingual bacterial preparation MV140 (Uromune) has the strongest placebo-controlled efficacy signal, with marked reductions in recurrence reported in women with rUTI, although it remains unlicensed in the United Kingdom. OM-89 (Uro-Vaxom), an oral bacterial lysate, has the longest clinical history and a broad evidence base, but findings across more recent studies are variable and access remains limited. Other approaches, including vaginal mucosal vaccines, intramuscular polyvalent preparations, and extraintestinal pathogenic *Escherichia coli* (ExPEC) conjugate vaccines, have shown mixed or disappointing results, highlighting the challenges of translating immunogenicity into meaningful clinical benefit.

Conclusions and Relevance: Immunoprophylaxis is no longer a fringe concept, but it is not yet ready for routine adoption in UK practice. For clinicians, vaccines should currently be positioned as a late specialist or research-pathway option within a stepped prevention approach, after confirmation of recurrent uncomplicated UTI, exclusion of red flags such as possible malignancy or structural pathology, optimization of behavioral and hormonal strategies, and consideration of established nonantibiotic and antibiotic prophylaxis options. Future studies should use standardized rUTI definitions and patient-centered outcomes, including recurrence reduction, antibiotic avoidance, quality of life, safety, and cost-effectiveness.

Keywords Recurrent urinary tract infection, immunoprophylaxis, vaccine, MV140, antimicrobial stewardship

Introduction

Urinary tract infections (UTIs) are a familiar clinical problem across primary care, acute medicine, and urology. They are also a major health system burden: in 2017–2018, the

estimated total cost for nonelective admissions for kidney infection or UTI in England was £386.1 million.¹

Recurrent UTI (rUTI) is usually defined as at least 2 symptomatic episodes in 6 months or at least 3 in 12 months.² In an English population-based survey, 37% of women reported at least 1 lifetime UTI, 29% reported more than 1 UTI, and 3% reported 3 or more UTIs in the previous year.³ For global context, the burden of UTI overall remains substantial and is increasing, particularly among women and older adults; however, recurrence-specific epidemiology is less standardized internationally, and a recent systematic review found marked heterogeneity across rUTI studies from multiple countries, limiting the reliability of any single worldwide incidence estimate for rUTI itself.⁴

This review focuses on recurrent uncomplicated UTI in noncatheterized patients. Catheter-associated UTI and

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urosepsis overlap microbiologically with rUTI but involve distinct diagnostic, preventive, and treatment pathways; they are therefore addressed here only briefly for context.

Current Prevention Options and Their Limits

For many patients, the prevention pathway begins with advice on hydration, bladder habits, and addressing modifiable risk factors. For postmenopausal women, vaginal estrogen is a well-established option. Other commonly used measures, including cranberry products, have mixed evidence and can be difficult to translate into predictable, sustained benefit.⁵ D-mannose is widely used but is not currently supported by sufficient trial evidence to recommend routinely.

When nonantibiotic measures fail, clinicians often reach for low-dose antibiotic prophylaxis. This can be effective, but it may cause adverse effects, microbiome disruption, and antimicrobial resistance. Trimethoprim resistance among urinary *Escherichia coli* isolates in England has been reported around the 30% range in community data, challenging its role as an empirical option in many settings.⁶

Other nonantibiotic approaches are gaining visibility. Methenamine hippurate is now explicitly recommended in updated National Institute for Health and Care Excellence (NICE) guidance for some women as an alternative to daily antibiotic prophylaxis.⁷ At the specialist level, intravesical glycosaminoglycan (GAG) layer replenishment (eg, hyaluronic acid with or without chondroitin sulfate) is included in European guidance as a possible option after less invasive measures, while acknowledging that further confirmatory trials are needed.⁸

Vaccines for rUTI: New Momentum for an Old Idea

This brings us to the “new kids on the block”: vaccines and vaccine-adjacent immunoprophylaxis. Although immunostimulant strategies for rUTI have been explored for decades, recent trials and the global drive to reduce antibiotic exposure have renewed interest in vaccination as an antibiotic-sparing option.^{9–11}

The appeal is straightforward. Vaccines aim to prime the immune system against uropathogenic organisms or shared antigenic structures, potentially reducing recurrences without prolonged antibiotic exposure. Several candidates use different routes of administration, including oral, sublingual, intramuscular, and topical/vaginal approaches as shown in the Table.

What Does the Evidence Show and What Should We Conclude?

If you strip the hype away, the current rUTI “vaccine” landscape is really four different stories: (1) MV140 (Uromune), which has the cleanest placebo-controlled signal; (2) OM-89 (Uro-Vaxom), which has the longest trial history; (3) older polyvalent/mucosal approaches (often discussed under Solco-Urovac/Urovac/StroVac), for which the evidence is more fragmented and harder to translate; and (4) newer extraintestinal pathogenic *E coli* (ExPEC) conjugate vaccines, which are biologically sophisticated but have not yet delivered clinical impact at scale.

Table Commonly Discussed Immunoprophylaxis Candidates for rUTI and Their Routes of Administration

Candidate	Route	Composition/concept	Evidence status
MV140 (Uromune)	Sublingual spray	Whole-cell inactivated bacteria: <i>E coli</i> , <i>Klebsiella pneumoniae</i> , <i>Proteus vulgaris</i> , <i>Enterococcus faecalis</i> (25% each)	Placebo-controlled RCT shows marked reduction in recurrences in women; unlicensed in the United Kingdom ¹²
OM-89 (Uro-Vaxom)	Oral capsule/tablet	Bacterial lysate derived from 18 strains of <i>E coli</i> ; typically taken daily for 90 days	Older RCTs show fewer recurrences vs placebo; newer evidence suggests smaller/variable effect; unlicensed in the United Kingdom ^{13–15}
Solco-Urovac and other mucosal/topical strategies	Vaginal suppository (mucosal); related IM product: StroVac	Inactivated uropathogenic bacteria delivered parenterally or via mucosa to stimulate systemic and/or local immunity	Small phase 2 vaginal studies suggest benefit mainly with boosters; no definitive phase 3 program; related IM StroVac RCT showed no overall reduction in UTIs ^{16–18}
ExPEC conjugate vaccines (eg, ExPEC9V programs)	Intramuscular injection	O-antigen conjugate vaccines targeting ExPEC serotypes; developed primarily to prevent invasive <i>E coli</i> disease	Phase 3 E.mbrace stopped for futility (insufficient efficacy for primary end point); no new safety signal reported ¹⁹

Abbreviations: ExPEC, extraintestinal pathogenic *Escherichia coli*; IM, intramuscular; RCT, randomized clinical trial; rUTI, recurrent urinary tract infection; UTI, urinary tract infection.

MV140 (Uromune) is the current standout on efficacy signal. In a multicenter randomized, double-blind, placebo-controlled trial in women with rUTIs, recurrence outcomes separated sharply from placebo: the median number of UTIs during follow-up was 3.0 with placebo vs 0.0 with MV140, and over the 9-month efficacy period following 3 months of treatment, UTI-free rates were about 25% (placebo) vs 56%–58% (MV140).¹² In the United Kingdom, however, MV140 remains unlicensed, so use tends to sit in specialist/local unlicensed-medicine pathways rather than routine primary care; early UK experience is supportive but inevitably more vulnerable to selection and reporting bias than placebo-controlled trials.^{20,21}

OM-89 (Uro-Vaxom) is “good” in a different way, not because 1 trial is spectacular, but because the evidence base spans multiple randomized placebo-controlled studies and decades of clinical use. In 4 classic randomized clinical trials (RCTs; 1990–2005), the mean number of UTIs during follow-up was roughly halved with OM-89 vs placebo (eg, 0.47–0.84 vs 1.28–1.76 episodes per patient; absolute reduction, approximately 0.44–0.94), and the proportion experiencing ≥ 1 recurrence fell by about 15% to 45% absolute, depending on the trial.^{22–25} A 2009 meta-analysis concluded that OM-89 reduced recurrence risk overall, but heterogeneity and trial quality were persistent issues.¹³ More recent synthesis suggests that the apparent effect has diminished in newer trials, and a large 2015 study of a modified preparation (OM-89S) reported no difference vs placebo.^{14,15} UK real-world data point in the same direction as the older trials, with fewer UTIs in the year after treatment compared with the year before.²⁶ The reason it has not become routine in the United Kingdom is mostly practical: unlicensed status, variable access and commissioning, and an evidence profile that does not consistently answer current commissioning questions (durability, clear patient selection, and antibiotic-sparing value).

The older polyvalent whole-bacteria vaccines illustrate both the promise and the messiness of this field. Routes and formulations vary (mucosal/vaginal vs intramuscular), booster schedules differ, definitions of recurrence are inconsistent, and placebo responses can be large. In 2 phase 2 vaginal Solco-Urovac/Urovac trials, boosted regimens reduced the proportion with any recurrence over 6 months from around 83%–89% (placebo) to ~45%–54% (vaccine + boosters), while primary immunization without boosters showed little to no benefit.^{16,17,27} However, the product did not progress to robust phase 3 programs and availability became limited, while a later placebo-controlled RCT of an intramuscular polyvalent vaccine (StroVac) did not show a significant overall reduction in UTIs vs placebo over 12 months.¹⁸

ExPEC conjugate vaccines (eg, ExPEC9V programs) matter to the wider “UTI vaccine” narrative, but the nuance is important. These programs were primarily designed to prevent invasive ExPEC disease (eg, bacteremia/sepsis) in older adults rather than uncomplicated rUTIs. The major phase 3

program (E.mbrace; ExPEC9V) was discontinued in February 2025 after an independent interim analysis concluded it was unlikely to meet efficacy end points; no new safety signal was reported.¹⁹ For rUTI prevention, the message is not “vaccines do not work”; it is that even a high-quality conjugate platform can fail if immunogenicity does not translate into real-world disease reduction.

Overall, immunoprophylaxis for rUTI is no longer fringe, but it is not ready for blanket adoption. Right now, MV140 has the clearest clinical efficacy signal, OM-89 has breadth but adoption barriers, older polyvalent approaches remain too heterogeneous, and ExPEC conjugate vaccine setbacks remind us that “biologically plausible” is not the same as “clinically effective.” The next step is straightforward: pragmatic trials in UK-relevant populations with end points that matter to patients and antimicrobial stewardship (episodes, antibiotics avoided, quality of life, and cost), alongside licensing and commissioning routes that can make successful options accessible.

Implications for Clinician Readers

A practical stepped prevention pathway is shown in the Figure. The pathway is intended to support clinicians at the point of first contact by separating patients who need further assessment or referral from those who can be managed within a recurrent uncomplicated UTI prevention pathway.

The first step is to confirm that the patient meets the definition of rUTI, usually 2 or more symptomatic episodes in 6 months or 3 or more episodes in 12 months, and to document symptom pattern and urine culture results where appropriate. Clinicians should also consider alternative diagnoses and red-flag features, including hematuria, persistent sterile pyuria, pelvic pain, weight loss, or recurrent culture-negative symptoms, as these may indicate malignancy or other structural pathology rather than recurrent uncomplicated infection.

Once complicated UTI, catheter-associated UTI, upper-tract infection, and structural or functional abnormalities have been considered, prevention can be approached in a stepwise manner. This includes addressing reversible risk factors, discussing behavioral measures, and considering vaginal estrogen in peri- or postmenopausal patients where appropriate. Evidence-based nonantibiotic options, particularly methenamine hippurate, should be considered before moving to self-start, postcoital, or continuous antibiotic prophylaxis.⁷ Where specialist pathways exist, intravesical GAG replenishment may be considered for selected patients after less invasive strategies have failed.⁸

Finally, when patients ask about “UTI vaccines,” honest counselling matters. A balanced message is possible: early trial signals for some immunoprophylaxis approaches are promising, but long-term durability, comparative effectiveness, cost-effectiveness, and licensing remain uncertain in the UK context.

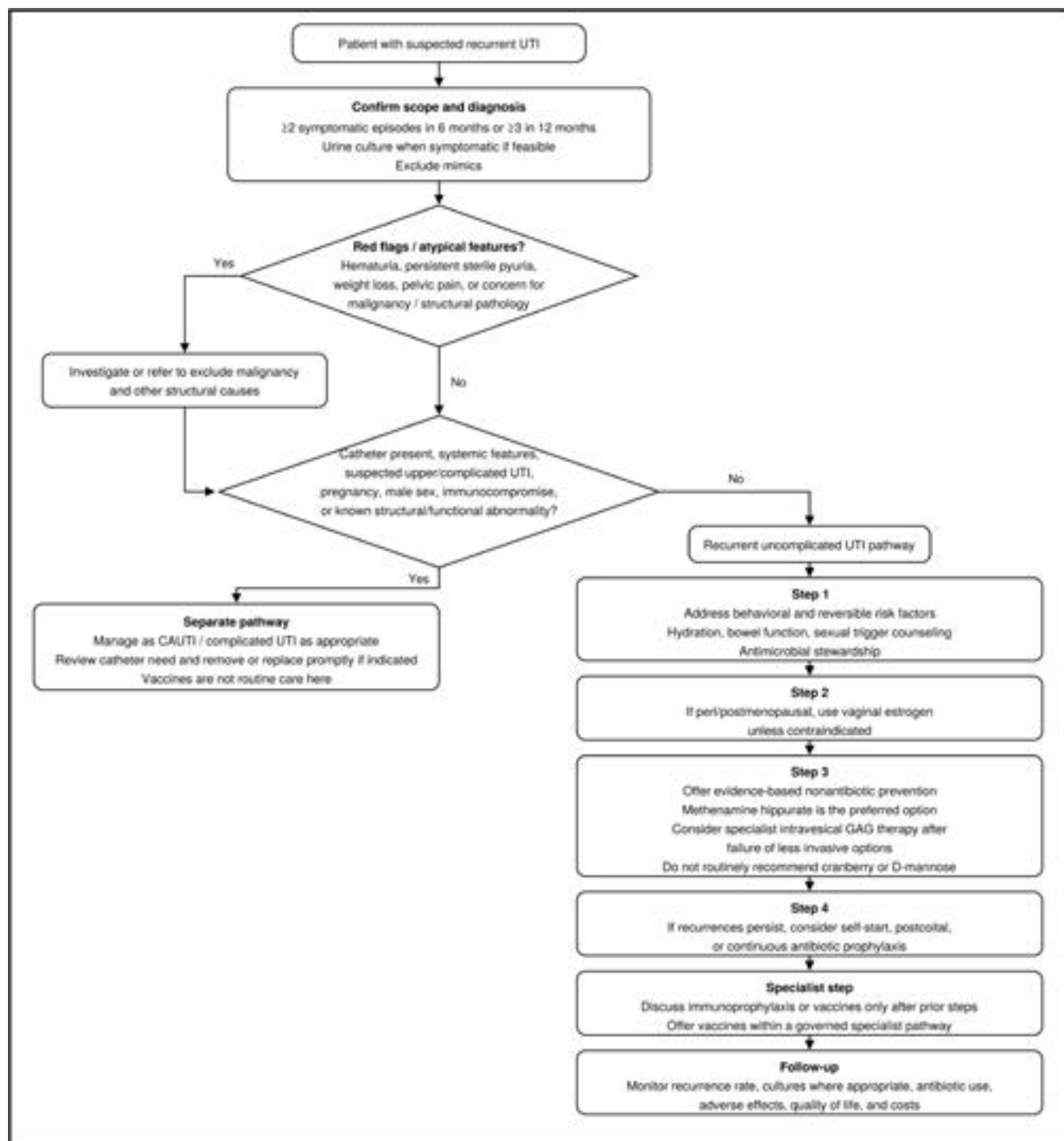


Figure Stepped prevention pathway for recurrent uncomplicated UTI, including exclusion of red flags and positioning of immunoprophylaxis as a late specialist option. CAUTI, catheter-associated urinary tract infection; GAG, glycosaminoglycan; UTI, urinary tract infection.

Conclusion

Vaccines and immunoprophylaxis are not a quick fix for rUTIs, but they represent a credible attempt to move prevention beyond reliance on long-term antibiotics. Pragmatic studies are

now needed with clear, standard rUTI definitions and (where possible) culture confirmation, focusing on outcomes that matter: recurrences, antibiotics avoided, quality of life, harms, and cost-effectiveness. If that evidence matures, “sprays and tablets” may become a genuine part of the rUTI prevention toolkit.

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Towards a Globally Recognized Physician Associate Role: Standardization, Disaster Readiness, and Systems Integration

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Abstract

Importance: Health systems worldwide face persistent workforce shortages, increasing disaster frequency, and widening gaps in access to essential medical and surgical services, particularly in fragile, resource-poor regions. Advanced practice clinicians, including physician associates (PAs), represent a highly scalable workforce solution; however, the absence of standardized role definitions, uniform training frameworks, and mutual regulatory recognition severely limits their effective deployment across global health systems.

Observations: Drawing on policy analysis, workforce literature, and practice-informed insights from emergency medicine, complex surgical trauma, disaster response, mobile health delivery, indigenous health services, and humanitarian missions in Ukraine, Uganda, Tanzania, Guatemala, and Panama, this article highlights how cross-border variability in PA recognition undermines operational interoperability, operative readiness, and overall health system resilience.

Conclusions and Relevance: Harmonized educational competencies, ethical governance structures, and strategic international collaboration could enable medical and surgical PAs to contribute more effectively to surge capacity, perioperative care, and routine and disaster relief in resource-constrained environments. Establishing a globally coherent PA framework represents a pragmatic, high-impact strategy to strengthen comprehensive health systems, optimize surgical and medical deployment, and improve global patient care outcomes while fully respecting national regulatory autonomy. This article examines the case for a globally recognized PA framework grounded in competency-based standardization rather than rigid, title-based national regulation.

Keywords Physician assistant, physician associate, global health care, disaster relief, crossing borders

Introduction

Poland first used feldshers, or mobile medical practitioners, in the 18th century to extend near-physician-level medical care to rural areas and to address health care needs during war-time.^{1,2} Due to geopolitical conflict, military operations disrupted the health care system within Poland. Poland lost many physicians at this time, and rural populations became more isolated from medical care. The feldsher served as a model to supplement medical work, including working directly with

physicians and providing care to foot soldiers in combat.² This concept was also a model for the physician associate (PA) profession in the United States.²

The PA profession was developed in the United States during the 1960s by Dr Eugene Stead. Liberia introduced PAs in the same year.³⁻⁷ During World War II, physicians could not keep pace with the increased demand for primary care.^{6,8-11} Over the subsequent decades, due to these physician shortages, several advanced health care provider professions have been developed in the United States. However, health care disparities and access issues do not exist solely in the United States.³ Global health systems are under unprecedented strain.^{12,13} Global disasters are becoming more frequent, health care worker (HCW) shortages are at critical levels, and the demand for advanced-skills-trained international HCWs is increasing.^{12,13} These disasters frequently cross geopolitical boundaries and generate medical needs that may go unmet. The global HCW workforce urgently needs restructuring to meet these medical demands.

Demographic transitions, epidemiologic shifts, climate-related disasters, armed conflict, and persistent inequities in

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access to care have converged, exposing precipitous weaknesses in health care workforce capacity. Recent large-scale public health emergencies and complex humanitarian crises have further underscored the fragility of existing models and the consequences of insufficient surge-ready clinicians.^{12,13} Although physician and nursing archetypes dominate policy discourse, less attention has been paid to the potential role of advanced practice clinicians, particularly PAs, within a resilient, adaptable global workforce.

Physician associates are trained to deliver comprehensive medical care across a range of clinical settings under physician-led or physician-supervised models.^{4,14,17} Most countries that adopt the PA profession use the US-developed framework as their model.⁶ In the United States, PA programs last 2 to 3 years with a terminal master's degree. The doctoral degree for PAs is also gaining traction as more PAs become interested in furthering their education. Before matriculating into PA school, individuals complete medical prerequisite courses, and many have thousands of hours of patient care experience. Becoming a PA requires successful completion of core classes, standardized examinations, and clinical rotations lasting several weeks at a time. The focus of PAs' training is in primary care, and their generalist training allows them unique career flexibility. Physician associates have a high degree of autonomous practice—they diagnose, perform physical examinations, take histories, and treat patients in collaboration with physicians.⁶ In certain areas of the world, such as sub-Saharan African countries, access to safe surgery is limited due to the low number of physicians per population. The prevalence of high reproductive health-related morbidity and mortality in these areas led to the training of clinical officers to perform cesarean deliveries.¹⁸

Over time, various other countries, including Australia, Canada, Germany, India, the Netherlands, and South Africa, have adopted PAs in their health care systems or have roles similar to those of PAs.^{6,7,19} The United Kingdom introduced PAs in 2003 and has more published data on PAs than any other European country.^{6,19} The PA profession continues to grow globally. However, with any growth, new challenges, such as standardizing the educational model and accreditation process, can arise. This process has taken decades to achieve in the United States, and efforts to advocate for the profession in its country of origin continue. Filling this knowledge gap by educating the public about the role of PAs and their scope of practice (SOP) will facilitate this global legislative initiative.^{6,7,19}

This review aims to answer the question of the global impact of PAs in clinical practice and argues that it is time to consider a globally recognized PA role framework—one that prioritizes competencies, ethics, and interoperability over rigid title-based regulation. It seeks to advocate for expanding the profession to eliminate global health disparities. Such a framework could enhance disaster response readiness, support underserved populations, and strengthen health system resilience worldwide.

Methods

A review was conducted over 2 years by 2 authors using literature collected from 4 databases—PubMed, MEDLINE Ultimate, CINAHL Plus with Full Text, and Google Scholar. Sources included peer-reviewed literature on global health workforce policy, disaster medicine, advanced practice clinician integration, and humanitarian health systems.^{12,13,20,22} Inclusion criteria, such as physician assistants or PAs, were used. Physician associates' contributions in disaster response and/or surgical settings and/or the use of PAs internationally, and full-text publications were also among the inclusion criteria. Non-English studies were excluded. Relevance was determined by title matching the articles' inclusion criteria, followed by abstract screening. Due to the lack of recent literature on this topic and to obtain data spanning a wide range of PA history, the 5-year filter was removed to complete the search.

The literature review includes mixed-methods studies, case studies, systematic reviews, and other study types. The literature most commonly evaluates the impact of PAs' roles using work logs, semistructured interviews, surveys, and direct observations. Gray literature from international organizations, professional associations, and governmental bodies was also reviewed to contextualize regulatory and policy environments. In addition to literature synthesis, the analysis was informed by one of the author's professional experiences across emergency medicine, trauma and critical care, mobile and community-based health care, federal civilian health systems, indigenous health services, and humanitarian medical missions in Ukraine, Uganda, Tanzania, Guatemala, and Panama. These contexts provide real-world insight into workforce interoperability challenges, SOP variability, and the operational realities of delivering care in austere and crisis-affected settings.

Thematic analysis was conducted during the article evaluation to assess the use of PAs and similar health care professionals. Themes were identified and compared for similarities found in multiple sources. Studies were examined for validity and generalizability according to the frameworks described by Creswell and Creswell²³ and Greenhalgh and Dijkstra.²⁴

Results

In this literature review, 43 sources were identified as meeting the inclusion criteria. Including the United States, 18 countries have adopted the PA career. Professions comparable to PAs exist in more than 50 countries with different titles; these professions have similar job duties but potentially varying SOPs comparable to those of PAs in the United States.^{3,5,7,19} Several studies have demonstrated that patient care delivered by PAs is of the same or higher quality as that of physicians,

that patients are satisfied with their care, and that access to care improves with their use. Although specific studies have used various markers, such as patient satisfaction and outcomes, PAs have been shown to deliver care equal to or superior to that of their physician colleagues.^{5,14,25-29}

A review of the classification of HCWs in the International Standard Classification of Occupations (ISCO) reveals that neither the World Health Organization (WHO) nor the World Medical Association lists a partnership, alliance, board member, or working group member with a PA title or PA-like role.^{20,21} A clear definition of the PA's role is needed to promote the inclusion of the PA profession in the global HCW pool. The profession has grown substantially in the United States over the past 50 years in terms of number and SOP.¹³ Many countries across the globe are also exploring the PA concept. These countries are adapting the PA concept to their specific needs regarding the medical provider shortage. These PA and PA-like roles provide physician-level care and comparable outcomes, predominantly through care delivered in accordance with US frameworks.¹⁴

A common barrier identified in the literature is limited understanding of PA roles. For example, in the United Kingdom, PAs are accepted by patients but are subject to different regulations regarding their SOPs, which can cause confusion. Physician associates in the United Kingdom do not have prescriptive authority as those in the United States do.^{6,9,27} Physician associates are not used effectively when patients do not understand what they can do for them. Similar themes identified in the literature revealed barriers to expansion, such as job title inconsistencies and limitations in SOPs.

Research shows that leveraging PAs offers a major opportunity to mitigate global health care shortages, enhance patient outcomes, and eliminate barriers to workforce planning and crisis response. Rapidly deploying clinicians during disasters or humanitarian emergencies requires absolute clarity on clinical competencies, supervision models, funding pathways, medical leadership, and legal authority. Currently, the absence of internationally recognized PA standards complicates credentialing, slows response times, and increases risk to both patients and providers. Without this clarity of roles, local authorities face confusion and ultimately miss critical opportunities to initiate medical deployments. This lack of clarity may also increase the potential for morbidity and mortality among patients in exigent circumstances.

Discussion

Barriers to Expansion

Job Title Fragmentation and Global Role Inconsistencies in Countries Adopting PAs. Despite the worldwide trend toward acceptance of the PA role and SOP, a formally

designated and globally recognized title for PAs and those who practice in PA-like roles has yet to emerge. Amid the projected HCW shortage, the role of PAs and their global analogs is often overlooked in workforce asset planning. Physician assistants/PAs and PA-like providers are often excluded from participating in global disaster response efforts because of the lack of an officially authorized PA title and SOP. The solution lies in the creation and acceptance of an internationally recognized PA title, along with a defined role and SOP specific to PAs' training and skills.

Multiple sources provide evidence of varying titles for nonphysicians who serve in roles similar to those of PAs in the United States.^{4,6,7} These may include the titles of clinical officers, clinical associates, medical assistants, health officers, health extension officers, feldshers, community health officers, health assistants, subassistant community medical officers, medical extension officers, and medical licentiates.²⁰ There are also differences in the regulation, education, and accreditation of PAs in other countries.⁷ Notably, New Zealand was recruiting PAs from the United States in mid-2020, and PA education is still under development there.⁴ Additionally, Taiwan officially halted the PA profession, and the status of PAs in Saudi Arabia is unknown, although Turkewitz et al⁶ reported that PAs were being used in emergency medicine in urban areas.

The term used in Poland, feldsher, further confuses the issue, as its definition varies by region.³⁰ Historically, the SOP, use, and public perception of feldsher in Eastern Europe have fluctuated significantly based on cultural contexts, chronological eras, and shifting physician supply.² The SOP of the feldsher, clinical officer, assistant medical officer, or clinical licentiate has subtle differences depending on local requirements, educational history, and implemented use by location or health care facility type. Most confusing, even to those within the profession, is the highly varied educational background required to enter these schools and the resulting training. For example, a clinical officer in one country cannot work as a licensed PA in another country; the titles and training are not reciprocal.^{31,32}

The inconsistency in the title further exacerbates confusion about the role of a PA. While a medical assistant in the United States serves strictly as support staff for health care providers, the title carries different clinical weights globally. For example, in Puerto Rico, they are referred to as *asistentes médicos*, whereas in Malaysia, "Medical Assistants" (officially known as Assistant Medical Officers) serve as autonomous clinicians, more closely aligned with the United States PA role.⁶ Countries in Africa presented the greatest variation in job titles and SOPs. Focusing on the worldwide legislation and regulation of the profession will help mitigate this barrier.^{5,6,19}

Disaster management stakeholders are responsible for dispatching medical aid to distressed communities. The numerous regional references for the PA and PA-like roles complicate

the selection process for determining which resources to dispatch.¹ A globally designated PA title condenses all of these references and encompasses the varied backgrounds from which PAs come.³³ Integrating the multiple name references into one title makes the dispatching process more efficient. In disaster situations, resources and ancillary clinical staff are frequently minimal. At the local level, the need for urgent medical aid far exceeds available resources.⁷

Across the globe, in individual countries, similar professions have been associated with the PA profession, with varying technical and clinical standards. Because the numbers and variety of the titles have become confusing, a definitive SOP for the PA profession globally has not been established. Without standardized frameworks, these contributions remain ad hoc and underused. Therefore, many health care supply agencies default to using nurse practitioners (NPs), physicians, and paramedics instead of PAs. Bypassing the PA role altogether has frequently been the path of least resistance for stakeholders seeking to avoid complex debates over professional nomenclature and SOP.

Scope of Practice. The limitations of a PA's SOP in some regions and an expanded SOP in others further demonstrate the need to clearly define the role to achieve equity, worldwide recognition, and respect for the PA profession.¹⁹ Furthermore, without a formal, standardized definition of the PA role, researchers cannot reliably isolate PA-specific contributions in large datasets. This effectively renders the profession invisible in the global health policy discourse. The lack of legislation and regulation of PAs globally remains a major challenge.⁶ Similar to the United Kingdom, the Netherlands introduced PAs to the workforce in the early 2000s. By implementing policies to extend PAs' SOP, acknowledging the profession legally, and increasing the number of subsidized opportunities, PAs in the Netherlands have seen tremendous growth since 2012, with an increase of 16% in the number of full-time equivalent PAs.³⁴

Certain countries in Africa, such as Tanzania, Malawi, and Kenya, use the concept of "task-sharing" or "task-shifting" to provide additional training to associate clinicians, who serve roles similar to PAs in the United States.^{18,35-38} Task-sharing addresses the extremely low physician-to-population ratio, which contributes to poor health outcomes in sub-Saharan Africa.^{18,35} Task-sharing with nonspecialists in Mozambique enables them to have a broader SOP in general surgery, obstetrics, and orthopedic surgery and may involve formal or informal experiences, such as "on-the-job" training.³⁶ Ashengo et al³⁶ noted that in Kenya, the SOPs for clinical officers are limited and do not include cesarean deliveries. Tanzania and Malawi both experienced a significant decrease in maternal mortality as a result of task-sharing practices.³⁵

Medical officers in Tanzania can be equated to physicians in the United States.³⁵ However, clinical officers are similar to PAs and have 3 years of medical training; they can diagnose,

prescribe, and perform minor surgeries. Assistant medical officers are clinical officers with 2 more years of clinical training and can perform surgeries such as cesarean deliveries.³⁷ Complications, such as maternal mortality in Tanzania, are complex problems with many contributing factors. On one hand, allowing assistant medical officers in Africa to perform emergency cesarean deliveries can significantly reduce maternal mortality and help improve global outcomes. Questions remain about whether allowing nonspecialists to participate in these complex tasks reduces the quality and effectiveness of the surgery. In Tanzania and Malawi, assistant medical officers performed emergency obstetric surgeries with the same clinical quality as general practitioners, resulting in comparable maternal and perinatal mortality outcomes. Maternal and perinatal complication rates remained unchanged between the 2 provider groups.^{36,37}

Ho et al³⁹ expressed concern about which procedures to share with nonphysicians because PAs and their equivalents are distinct from their physician colleagues. Expanding the SOP of PAs too broadly and granting complete independence from physicians contradicts the foundational principle of strong collaboration with physicians, a key factor in the success of the PA profession. Ngongo et al³⁵ reported that physicians are doubtful about the ability of associate clinicians to perform cesarean deliveries. Discussing the concept of optimal team practice (OTP), which is relevant to PAs in the United States, is beneficial to other countries as well. Optimal team practice promotes PA autonomy and responsibility without changing the SOP.⁴⁰ Sobel⁴⁰ emphasized the goals of OTP, such as reducing administrative constraints on PA practices and allowing them to have a voice in the regulation of the profession. This approach focuses on collaboration with physicians and the multidisciplinary teams for the benefit of patients. In adherence with OTP principles, the SOPs for a PA are flexible with respect to the degree of their training and experience.⁴⁰

The United Kingdom remains hesitant towards PAs' roles regarding SOP. Professor Gillian Leng recently made recommendations in a report called the *Leng Review*, and the government has agreed to implement them. They argue that the PA title is confusing for patients and will revert the PA title to "physician assistant" rather than "physician associate." If the United Kingdom's experience with the *Leng Review* demonstrates anything, it is that confusion over title and scope can cripple workforce integration.⁴¹ The American Academy of Physician Associates' response to the misrepresentation of PAs in the United Kingdom outlines an independent review of the manuscript and concludes that it lacked rigor, correlation, and statistical significance in support of its claims.⁴² This reality makes the call for a WHO definition all the more critical. Global standardization would provide the necessary regulatory clarity, leveraging the fact that PAs are fundamentally committed to collaborating with physicians within

defined SOPs. The UK government expresses distrust of PAs' qualifications to provide safe and effective patient care. PAs in the United Kingdom will also have increased oversight and will not be permitted to see undiagnosed patients independently. New PAs need to gain 2 years of experience in a hospital setting before working as primary care or mental health providers.⁴¹

The UK government's support for restrictions on PAs' SOP is concerning. Alternatively, partnering with influential organizations such as the WHO to regulate the PA profession through clear guidelines and a defined SOP can help achieve acceptance of PAs in countries where the profession is newly established. In locations where PAs cannot prescribe medications, a greater burden is placed on the physicians with whom they work. Gaining the support of physicians and the trust of community members at the local level could be vital to the growth of the PA model in diverse settings. Filling this knowledge gap by educating the public about the role of PAs and their SOP will facilitate this global legislative initiative.^{6,19}

Opportunities For Advancement

Critical Physician Shortage. International disaster demands an international response. New projections by the Association of American Medical Colleges⁴³ predict a shortage of up to 86 000 physicians in the United States by 2036. Although this number is smaller than the number predicted in their previous report, the burden remains significant when considering factors such as population growth and the large percentage of physicians entering into retirement. The global health workforce, consisting of doctors, nurses, midwives, dentists, and pharmacists, is projected to face a shortage of nearly 10 million workers by 2030.³¹ This shortage is concentrated in low- and middle-income countries (LMICs) in the Eastern Mediterranean and African regions.³¹ The PA profession can help minimize this shortage gap to the extent that international discussions embrace the PA model and SOP. A formally recognized WHO title for the PA profession would legally authorize government stakeholders to deploy PAs as a health care workforce resource, significantly enhancing international disaster response capabilities.^{5,13}

Bautista et al²⁵ predicted a surgeon shortage of 15 800 to 30 200 by 2034, underscoring the increased need for PAs in surgical specialties. In the United States, this burden is less obvious, as the physician-to-patient ratio is 11.93 to 1000. However, of 192 countries, 57 face a critical shortage defined by the WHO as a ratio of less than 2.28 per 1000.⁴⁴ In 2015, the WHO reported that an estimated 1 billion people worldwide lacked access to health care and predicted a global HCW shortage of 13 million by 2035.⁴⁴ Using PAs to close this gap in providing health care shows promise, as evidenced by the profession's success in the United States and other countries.

The implementation of PAs in a country usually begins with establishing a pilot program to address inequities in health care.^{7,44} Pilot programs can also foster a sense of ownership of the profession among the populations of the communities where PAs are introduced and developed, thereby furthering acceptance and trust as the culture shifts to embrace PAs as an effective health care solution.

The US educational and health care service model delivers the highest level of care, as evidenced by reproducible findings from patients who adhere to the care plans they receive from PAs.¹⁴ These patients are more likely to follow through with treatment plans, referral recommendations, medication prescribing, and routine preventive care, effectively decreasing the public health burden.^{14,15} Newly developing foreign programs with similar goals often send academic representatives and exchange students to the United States to learn about PA programs developed there.¹⁶ Many global academic systems recognize US standards for the PA educational model.¹⁷ Several countries model their programs based on examples from the US training programs for PAs. The Clinical Associate role in South Africa and the Medex Program in Guyana modeled their PA-like roles after highly successful site visits to the United States.⁴

The global integration of PAs will remain a challenge because no comprehensive educational model has yet been established. One reason for the inconsistency of such a model across countries may be the different political systems and financial resources of each country.¹⁰ The PA model is more likely to fail when there is government opposition or resistance from other HCWs or physicians. They are more likely to be successful when initially introduced into primary care settings to increase access in rural areas with higher-acuity health care needs.⁶ Compared with physicians, PAs' accelerated training period is an additional benefit advocating for their use.⁶

Wright et al¹⁰ reported that advanced practice provider (APP) students in the Netherlands receive government subsidies to pay tuition and are paid to work during their final year of training under the supervision of an experienced preceptor. This is a positive way to encourage the future development of PA programs; however, economic disparities in other countries may limit the ability to do this. Physician associates have been introduced to LMICs in South and Central America through volunteer medical work, and the potential for their implementation in countries such as Ecuador, Guatemala, Costa Rica, and Haiti could be further investigated through pilot programs. Allowing these programs offers a feasible long-term solution to address health disparities in those countries and helps meet surgical needs that have been met by roles similar to PAs in Africa.⁶

Patient Outcomes. The overarching theme of this review is that PAs deliver safe and effective care to patients in a variety of settings, including surgical teams. They provide continuity of care, increase productivity and revenue, and are

cost-effective.^{6,8,9,26,28,29,38} Research in the Netherlands compared two models of care—one with only physician-led care and the other with PAs leading care in place of residents. The majority of PAs involved in this study were practicing in surgical specialties, and patients reported better communication, continuity, and care on medical floors with PAs leading care in place of residents. Physician associates working in Dutch hospitals were found to be cost-effective, with a similar length of stay (LOS) for patients and quality of care compared to physicians.²⁸

Johal and Dodd²⁶ sought to examine the impact of PAs and NPs on surgical/trauma services and reported that their addition to the team led to improved operational efficiency, decreased cost and LOS, and increased satisfaction rates among patients and HCWs. Adding APPs to the surgical team also decreased stress and workload levels for the residents.^{25,26} The benefits of expanding the PA profession can be concluded when considering the dangers of physician shortages combined with increasing health care demands and an aging population. The COVID-19 pandemic further emphasized the need for robust health care systems worldwide, and as a result, the PA experience in other countries has drawn international interest.^{4,5,9,29,38,45}

In addition to clinical patient care, PAs are well-trained to implement health care delivery processes and perform leadership tasks for a medical team.¹⁶ In many regions of the world, there is a need for improved medical leadership and better health care delivery.⁷ A specific PA title designation could fortify delivery infrastructure for these areas. A clinical and managerial role of a PA in these regions would allow PA autonomy, especially in disaster situations.

Local authorities turn to more prominent stakeholders for support, requesting medical aid, including HCW personnel. Developing a designated title and a clear SOP would consolidate these numerous regional PA-like role references into a centralized global clearinghouse. Practitioners who meet the criteria for working in these areas can maintain their identification and certification credentials in a centralized database. International stakeholders, such as the WHO, must be ready to augment local disaster response efforts by maintaining a cadre of advanced-practice medical providers.⁵ This catchment can serve as a reservoir of HCWs qualified to respond to disasters. If the WHO officially consolidates these references under a single title, there will be a more robust pool of HCWs to draw on in times of need. The WHO can quickly draw on this database and effectively deliver aid to local authorities.

The strongest predictors of success in countries with PAs are having government support for developing PA training programs and focusing on adding them to the rural workforce to increase access to health care. Pilot programs conducted in European countries correlate with the successful implementation of PAs in the workforce; they increase awareness and knowledge of PAs' roles and help people see the value they can bring to patient care.⁶

Although government stakeholders historically designed the feldsher to address Poland's wartime and rural medicine

shortages, a global need for medical coverage in rural and underserved communities persists and is essential in disaster response readiness.² Throughout many areas of the world, individuals with varied backgrounds entering into clinical officership or licentiate may not require any previous clinical patient experience.⁵ To address this trend, it might be advantageous to use foreign-trained PAs to come to this country to serve in rural areas. For many of these individuals, it would be similar to working in their native country. This exception may provide an opportunity for higher education and pay for the foreign-trained providers, with the caveat that they work only in rural medicine in the United States.⁴⁶

Creating special interest groups, building international relations, and developing an international exchange program for new PA programs worldwide are part of sustaining a global identity and maintaining the highest standards of care in the PA profession. Greater frequency of conference presentations, heightened leadership positions, creation of a PA task force for international global identity, and formation of a representative body to lobby with the WHO are additional pathways to frame the PA tenet.^{5,46}

Limitations

Weaknesses identified in this literature review are inaccurate quantitative data in 1 study, possible bias in one study's sample selection, and possible competing interests in other studies. Due to the qualitative nature of this topic, conducting a randomized controlled trial or a blinded study is unlikely. The search strategy is not fully reproducible, and the inclusion and exclusion criteria are vague. This is, unfortunately, due to the lack of a global definition of "physician assistants."

Current health care data collection models have found isolating the PA profession's contribution to global disaster response challenging. There is no consistent international recognition of the training that allows PAs to provide high-quality, physician-like care and physician-level health care outcomes.¹⁵ Descriptors do not solely reflect the SOP provided by PAs.^{13,15}

The impact of the PA profession is best measured by the patients under their care, supervisors, and other health care professionals who work alongside PAs and cannot be blinded. The lack of a meta-analysis and heavy reliance on qualitative data are weaknesses; there is a great need for more quantitative research on this topic. The results of this review were triangulated to compensate for these deficiencies by incorporating mixed-methods and case-study designs. Data were obtained from 4 continents where PAs are currently used. Perspectives were analyzed in countries that still expressed hesitation to adopt the new role of PAs, as well as in those that were supportive of its implementation.

Conclusion

Civilian and military institutions internationally recognize nurses, dentists, pharmacists, and physicians as the primary clinical responders in disaster medical response teams. There are many barriers to introducing PAs in countries unfamiliar with the role. A globally recognized definition of the PA profession's role and SOP is needed to increase the provider pool of the global disaster health care workforce. Advancing the role of PAs and their SOP is a critical solution to advance medicine globally and reduce disparities caused by workforce shortages in areas where PAs do not exist, especially in LMICs. This review serves to enlighten international political leaders, legislators, and physicians about the potential of the PA career in their nations. Gaining support to develop educational models for PA training will involve collaboration with global organizations, such as the WHO, to support this effort. The most prominent international stakeholders, the WHO, the World Bank, the International Monetary Fund, and the International Association of Medical Regulatory Authorities, who address the global HCW shortage, overlook a potentially significant population of medical providers. Petitioning the WHO to officially define and formally recognize the PA title will allow PAs and those in PA-like roles to function to their greatest ability as valued participants in global disaster medicine.²⁰ The WHO and the ISCO recognize the NP as an authorized advanced medical provider with a defined SOP.²⁰ The ISCO must include the PA in its classification databank and recognize the PA as an advanced medical care provider with a defined SOP as well. The lack of a consistent global identity and SOP for the PA profession results in the exclusion of PAs as advanced medical providers globally. Expanding the role of the PA in surgical specialties globally will increase access to safe, timely care for patients. This initiative creates thriving, self-sustaining health care systems that not only transform the lives of those treated but also positively affect humanity as a whole across diverse settings.

Generative AI Use

During the initial preparation of this manuscript, the authors used Grammarly for proofreading. During the final preparation of this manuscript, the authors used Grammarly and Google Gemini to assist with proofreading, language polishing, and editing. After using these tools, the authors reviewed and edited the content as needed and take full responsibility for the accuracy and integrity of this publication's final content. Grammarly was used to evaluate any grammatical errors but no generative AI was used for content creation.

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The Symphony of Care: Physician Associates Multifaceted Role in Extracorporeal Membrane Oxygenation Program

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Abstract

As extracorporeal membrane oxygenation (ECMO) technology continues to expand, particularly after the COVID-19 pandemic, there is a critical need for organized ECMO programs. This presents unique career opportunities for allied health professionals. Our manuscript explores these possibilities. It outlines a roadmap for future organized ECMO programs, as well as education and manpower delegation pathways. This article focuses on physician associates in key roles by highlighting their skill sets.

Keywords ECMO, physician associate, mechanical circulatory support devices, ECMO specialists

Introduction

Extracorporeal membrane oxygenation (ECMO) is a type of life support used in the most critically ill patients with gas exchange or circulatory failure.¹ Previously believed to support heart and lung function, the use of ECMO currently covers numerous critical care adult and pediatric indications, including certain former contraindications such as trauma and septic shock. Such patients represent the most critically ill cohort presenting to the hospital. Mechanical circulatory support (MCS) devices and ECMO patient selection, cannulation, maintenance, and exit strategies have historically been managed by cardiovascular surgical teams owing to their clinical surgical profile and access to trained personnel such as physician associates (PAs), perfusionists, and nurses. However, with increasing critical care indications, especially after the COVID-19 pandemic, there has been an exponential increase in the number of ECMO cases worldwide. Hence, there is a pressing need for uniform training of all stakeholders in the nuances of ECMO expertise. India embarked on the ECMO journey over the past 10 years with sporadic centers mostly transplant centers with limited cases and limited success.²⁻⁴ However, after the COVID-19 pandemic, there has been an exponential increase in the number of ECMO centers globally (>750). India has also seen a sharp rise in the number of

centers offering ECMO services, percolating tier 2 cities as well. This opens the possibility of treating ECMO as an independent program owing to the myriad of trained personnel involved in its successful implementation, similar to a transplant program. In this descriptive review, we describe various stakeholders, their roles, and training for an ECMO specialist, with the PA at the center of the narrative.

Background

The ECMO program entails assembling all multidisciplinary stakeholders on a common platform to create pathways for training, execution, research, program evaluation, and development. In this article, we explore the role of the PA in the complex requirements of an ECMO program. With this objective, we first describe the various arms and personnel roles for ECMO patient care. We then review the latest PA curriculum to study the skill sets and training that are already part of the curriculum that makes PAs ideal team members for an ECMO team. We also conducted a literature search to study models that use allied health professionals, such as physician assistants, nurse practitioners, and perfusionists, as ECMO specialists for patient's clinical management and the program's overall pathway, research, and training objectives for uniform standardized care.

Discussion

The ECMO program can be divided into various arms for smooth workflow, appropriate resource allocation, and successful clinical management. In the Figure, ECMO pathways

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Figure The complex multifaceted nature of an extracorporeal membrane oxygenation (ECMO) program with focus on timely patient selection, cannulation, troubleshooting, and coordination for better patient outcomes

are divided into patient selection,^{5,6} cannulation, trouble shooting, and coordination.

ECMO indications are broadly categorized as heart failure, lung failure, critical care indications, and peritransplant care. Patients may be referred by cardiologists, pulmonologists, adult and pediatric cardiothoracic surgeons, adult and pediatric critical care specialists, emergency medicine physicians, and transplant teams. Patients who meet criteria for reversible gas exchange and circulatory failure should be escalated in the therapeutic window for mechanical support. With such a wide scope of service, institutions should organize their ECMO

pathways to include all relevant personnel involved in ECMO selection and activation.

ECMO cannulation requires expertise training and credentialling.⁷ Cannulation can be performed in any location, including ambulance and out of hospital; however, currently, for best outcomes with minimal complications, the cardiac catheterization laboratory, intensive care unit (ICU), operating room, and emergency department (ED) should have processes and pathways to initiate ECMO within the hospital. This approach is intended to avoid transferring critically ill patients and risking the loss of the window for successful

salvage. ECMO can be initiated surgically or by the percutaneous Seldinger technique. Because of the large cannula size and procedural urgency, cannulation complication rates are high; therefore, training triaging and follow-up of the cannulation site are required beyond decannulation and discharge. Personnel skilled in cannulation include physicians, intensivists, cardiac and vascular surgeons, and PAs.

Troubleshooting: ECMO patients are managed across diverse intensive care settings, including cardiothoracic, general, transplant, adult, and pediatric units. The management of these patients presents a unique dual challenge, requiring the precise integration of mechanical support and clinical care. When used optimally as a “safety net,” ECMO can achieve hemodynamic and respiratory stability in the most critically ill patients.

Furthermore, ECMO provides a therapeutic window for active rehabilitation while patients await organ recovery or transplantation, thereby potentially mitigating the morbidity associated with prolonged critical illness. Realizing these improved outcomes necessitates the strategic application of ECMO and MCS devices.

To ensure patient safety and minimize technology-related complications, ECMO teams must be vigilant, available, and highly trained in both continuous monitoring and rapid troubleshooting. This expertise is essential for clinical and mechanical optimization, as well as for the management of high-risk intra- and interhospital transport for diagnostic or therapeutic interventions. Consequently, this care pathway requires a dedicated, 24/7 presence of ECMO specialists. This versatile role may be filled by trained physicians or allied health professionals who possess comprehensive knowledge of critical care, clinical and administrative protocols, and perfusion science.

The current model of a typical ECMO team with its roles and responsibilities is listed in Table 1.

Coordination: Hesitation to implement ECMO as a life-saving intervention often stems from its labor-intensive, cost-intensive, and time-sensitive nature. In the absence of standardized clinical pathways, patients frequently miss the optimal therapeutic window, leading to preventable complications and poor clinical outcomes; this, in turn, diminishes institutional confidence in the technology.⁸

Much like complex transplantation services, a robust ECMO program necessitates seamless coordination across a multidisciplinary team—including physicians, surgeons, nursing staff, and financial administrators—and various hospital sectors, such as the ED, operating theatre, ICU, and supply chain management. Effective coordination requires clearly defined protocols regarding manpower roles and responsibilities, inclusion and exclusion criteria, and the strategic allocation of equipment and consumables.

To ensure clinical harmony, all relevant specialties must have access to uniform training that clarifies their role within the activation and maintenance cascade. This

Table 1 Roles and Responsibilities of Personnel in an ECMO Program

Member/ Designation	Role/Responsibility
ECMO program director	1. Chief coordinator of the program, directly and primarily involved in all aspects of the clinical course of treatment of the patient. 2. Organize and train the team and develop and oversee the program.
Cardiac/vascular surgeon	1. Perform ECMO cannulation and supervise physician associates during cannulation. 2. Perform daily checks of cannula and troubleshoot cannula-related complications. 3. Change configuration. 4. Determine exit strategies, including transplantation, VAD, and CABG. 5. Perform decannulation.
Anesthetist/ critical care intensivist/ pulmonologist/ cardiologist/	1. Patient selection. 2. ECMO initiation. 3. Supervise junior anesthetists/intensivists/perfusionists/physician associates in patient management. 4. Provide assistance during ECMO retrieval.
Perfusionist	1. Prime circuit. 2. Maintain checklist of consumables and ECMO machines. 3. Assist with care of ECMO machine and circuit during retrieval, initiation, configuration change, decannulation, transport, and mobilization. 4. Perform daily circuit and machine checks. 5. Be available for troubleshooting 24/7.
Clinical coordinator	1. Retrieval-related coordination with team. 2. Coordination with the parent hospital. 3. Manage logistics. 4. Coordination of all phases of ECMO care up to discharge and follow-up to ensure continuity of care. 5. Maintain the data associated with risks, outcomes, etc.
Cardiothoracic physiotherapist	1. Provide chest physiotherapy and mobilization during ECMO under the supervision of ECMO specialists (physician, perfusionist, or PA) 2. Provide post-ECMO rehabilitation from critical illness
OT nurse/ ECMO ICU nurse	1. Assist the surgeon during ECMO procedures in OT or bedside in ICU 2. Manage the patient, including assessment, complex nursing procedures, administration of medications, monitoring for complications, managing patient's pain, and maintaining strict asepsis.
ECMO financial SPOC	Address financial counselling and pathway for ECMO and advanced ICU care of critically ill patients.

Abbreviations: CABG, coronary artery bypass grafting; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; OT, operating room; PA, physician associate; SPOC, single point of contact; VAD, ventricular assist device.

requires cross-disciplinary education; for instance, nursing staff should gain proficiency in perfusion science, and vice versa. Furthermore, similar to transplant programs, rigorous research, data collection, and morbidity and mortality assessments are essential for continuous program evaluation and quality improvement.

Services such as extracorporeal cardiopulmonary resuscitation, extracorporeal donation after circulatory death, and mobile ECMO transport require 24/7 availability of trained personnel. Finally, post-ECMO care should be viewed as a continuum; survivors require long-term follow-up within specialized heart or lung failure and peritransplant clinics. There is an urgent need to integrate heart failure programs more deeply with existing ECMO and transplantation services.

According to Extracorporeal Life Support Organization (ELSO) guidelines, an ECMO specialist must master specific domains to ensure high-quality patient care.¹

- Clinical knowledge and physiology:
 - Deep understanding of cardiopulmonary physiology and how the ECMO circuit interacts with native organ function.
 - Expertise in anticoagulation management, including titration of heparin and monitoring of coagulation parameters (eg, ACT, aPTT).
 - Identification of indications and contraindications for different support modes, such as venoarterial (VA) and venovenous (VV) ECMO.
- Technical and mechanical proficiency:
 - Circuit management: Ability to perform safety checks, prime the circuit, and manage components such as the oxygenator and pump.
 - Troubleshooting emergencies: Immediate response to life-threatening issues such as air embolisms, pump failure, membrane lung failure, or accidental decannulation.
 - Optimization: Titrating blood flow and sweep gas to meet specific oxygen and carbon dioxide targets.
- Operational and procedural skills:
 - Safe transport: Protocols for maintaining circuit integrity and patient stability during movement within or between hospitals.
 - Team collaboration: Effective communication within a multidisciplinary team, often using structured tools such as ISBAR for handoffs.
 - Rehabilitation support: Coordinating with physical therapy to facilitate early mobilization while on mechanical support.
- Training and certification standards:
 - Completion of high-fidelity simulation training covering essential emergency scenarios.
 - Maintaining a minimum number of “pump hours” (eg, 56 hours per year) and undergoing regular recertification (typically every 3 years).

Role of PA in an ECMO Program

The PA's training provides a unique blend of vascular, coordination, and technical expertise. Hence, the potential to be vital providers of the ECMO training and execution team.

Curriculum and Role of PA in Health Care

In India, the PA cadre was introduced in 1992 to address the shortage of health professionals, particularly in fields such as cardiology and cardiothoracic surgery. More than 130 institutions in India offer PA programs, affiliated with around 25 universities, both public and private. An estimated 10 000 PAs are currently practicing in India, predominantly in private health care institutions and tertiary care centers.^{9,10}

“Physician Associates are healthcare professionals trained in a medical model who practice medicine as part of a healthcare team. They are qualified and competent to provide preventive, diagnostic, and therapeutic services under the supervision of a physician.”⁹

Role of PA in Complex Multidisciplinary Programs

The PA curriculum is a comprehensive theory and practical knowledge of all aspects of medicine and surgery. The curriculum also focuses on aspects of health care management, knowledge of research, quality in health care, and ethical issues.

PAs in India have been actively involved in cardiac sciences. Their curriculum includes most aspects of adult and pediatric critical care. The skills included in the curriculum that are essential for an ECMO program are presented in Table 2.

PAs possess a versatile blend of surgical and critical care skills that make them ideal for ECMO programs, often serving as ECMO specialists or advanced practice providers who bridge the gap between surgeons and bedside staff. In the United Kingdom, more than 84 000 allied health professionals with a range of skills and expertise play key roles within the National Health Service, working autonomously, in multi-professional teams in various settings.^{11,12}

Advanced Procedural Competency

- Cannulation and decannulation: PAs are trained in ultrasound-guided vascular access and the Seldinger technique, which are essential for both percutaneous and surgical cannulation and the subsequent safe removal of cannulas.

Table 2 Elements of the PA Curriculum and Training Relevant to the ECMO Program.

Topic	Depth of knowledge	Potential role in ECMO program
Cardiovascular disorders	Basic principles: Understanding heart anatomy, physiology, and pathophysiology Common conditions: Hypertension, coronary artery disease, heart failure, and arrhythmias Clinical evaluation: History and physical examination for cardiovascular conditions Diagnostic tests: electrocardiography, echocardiography, stress testing, and blood tests Management strategies: Pharmacologic management, lifestyle modifications, catheter-based interventions, surgical interventions, and chronic disease management Long-term management of hypertension, coronary artery disease, and heart failure	• Identify patients with heart failure and circulatory failure • Formulate treatment options • Optimizing clinically • Running appropriate diagnostics • Formulate exit strategies
Respiratory disorders	Basic principles: Respiratory physiology, pulmonary function, and gas exchange Common conditions: Asthma, COPD, pneumonia, tuberculosis, and interstitial lung disease Diagnostic tests: Pulmonary function tests, chest radiography, computed tomography, arterial blood gas analysis Management strategies: Pharmacologic treatment, oxygen therapy, mechanical ventilation	• Identify patients with respiratory failure • Formulate treatment options • Optimizing clinically • Running appropriate diagnostics • Formulate exit strategies
Critical care medicine	Basic and advanced concepts of critical care medicine Common critical care conditions such as respiratory failure, shock, sepsis, and multiorgan failure Monitoring: Diagnostics and devices Management of clinical conditions: Of complex multisystem diseases Management of nonclinical aspects: ethical and legal aspects of critical care, including end-of-life care and communication with families	• Identify critical care ECMO indications • Formulate treatment options • Optimizing clinically • Running appropriate diagnostics • Formulate exit strategies
Miscellaneous	Emergency medicine: Trained in basic life support and advanced cardiac life support in cases of cardiac or respiratory arrest. Coordinate emergency transport, ensuring smooth handoffs to higher medical centers or specialized care Surgical training: Assist as first or second assistant in surgical procedures (eg, cardiac surgery) Administrative: Coordinate referrals, maintain communication between specialists, maintain accurate and up-to-date patient records, and assist in reviewing and updating practice protocols to improve patient outcomes Research: Clinical research, medical training, and evidence based practice	• Resuscitation • Transport • Cannulation • Coordination • Program improvement

Abbreviations: COPD, chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygenation; PA, physician associate

- **Surgical proficiency:** Many PAs have background experience in cardiovascular surgery, providing the motor skills necessary for cut down for vascular access, suturing, managing surgical bleeding, and performing bedside procedures such as tracheostomy and chest tube insertion.
- **Circuit management:** All stakeholders who manage ECMO require training in circuit management and clinical and mechanical troubleshooting. PAs can be trained to troubleshoot mechanical failures, such as pump thrombosis or

raceway rupture, and circuit deairing in case of massive air embolism.

Critical care decision-making, hemodynamic interpretation of complex data from pulmonary artery catheters and 2-dimensional echocardiography to adjust ECMO and inotropic support based on the patient's changing physiology, management of anticoagulation, and weaning of support are all part of the PAs scope of service under physician guidance.

Allied Health Personnel

PA-Led Donor Management and Retrieval Model: This is an internationally tested model in which PAs are trained to manage the entire process of donor evaluation, cannulation, and transport for organ recovery, particularly in lung and heart transplantation. A study showed that a PA-led recovery model reduced the time commitment of attending surgeons on donor runs from 57.5 to 10.8 hours/month while maintaining equivalent 30-day survival rates (96.9% PA vs. 96.3% non-PA). This model is used for high-volume transplant centers to manage staff workload and maximize organ utilization.¹³

The “ECMO Specialist” Model (ICU-Based): PAs operate within a team-based, structured environment that includes intensivists, surgeons, perfusionists, and nurses.

PAs act as dedicated “ECMO specialists” within the ICU, managing the day-to-day operation of the circuit. While nurses often manage the patient and traditional ICU care and perfusionists maintain the circuit on daily rounds, PAs are often involved in the initial bedside cannulation and are responsible for troubleshooting circuit issues, managing anticoagulation, and performing daily, or hourly, rounds on ECMO patients along with the ECMO physician, surgeon, or cardiologist. This model has been shown to be safe, cost-effective, and provides high-quality care for VA and VV ECMO patients.

Rapid Response/Transport Team Model: PAs are key members of specialized transport teams for initiating ECMO in the ED or at outside facilities. For timely initiation in critically ill patients, a hub-and-spoke system with shock call activation and coordination between transplant or regional centers and referral centers has led to better outcomes in heart failure. Such shock teams have led to an improved in-hospital and long-term survival.¹⁴

Interdisciplinary coordination can be handled by PAs as the primary liaison between all clinical and management stakeholders. They would be responsible for standardized protocols and clear communication during high-stress handovers. Their role would involve educating families on the risks and benefits of ECMO and helping them navigate difficult ethical decisions regarding goals of care.

Key Components of Successful PA-Run Programs

Institutional Commitment: Success requires a “physician champion” or leader to build the program, backed by hospital support. PAs must undergo specialized, often simulation-based training (eg, ECMO specialist training course, 40+ hours of training and supervised patient care). Implementation of clear, actionable protocols (eg, using ELSO guidelines) is necessary for a successful PA-run model.

Cost and Resource Efficiency: PA integration significantly shifts the financial and operational structure of ECMO

programs by moving toward a more flexible, cost-efficient specialist model compared with the high-overhead traditional physician- or perfusionist-led model.

Operational Integration Models¹⁵

- **Specialist Model (PA-Run):** PAs function as “ECMO specialists,” managing the circuit and patient physiology simultaneously. This model often eliminates the need for 24/7 bedside perfusionists, with perfusionists instead serving as consultants for complex circuit issues.
- **Traditional Model (Perfusionist-Led):** Requires a dedicated perfusionist at the bedside for the duration of the ECMO run, in addition to the standard critical care team.
- **Dual-Provider Model:** A common hybrid in which PAs manage the medical aspects (cannula care, monitoring, and clinical trouble shooting) while a specialist or perfusionist handles the mechanical circuit.

Financial and Logistic Implications

Programs with fewer than 10 cases per year and for short runs (eg, 4 days for VA-ECMO) do not incur added cost in terms of manpower compensation for ECMO management.¹⁶

However, post-COVID-19, the respiratory indication for ECMO runs average approximately 10 days to more than 30 days. This has made the specialist model more cost effective, in which each stakeholder is trained to care for ECMO patients while an ECMO specialist ensures training and coordination. The ECMO specialist model augments the efficiency of each stakeholder without burdening them with extra work while ensuring patient safety. The ECMO specialist role can be physician or any allied health personnel.

Strengths of This Review

This is the first review of its kind to introduce PAs to the concept of ECMO as a comprehensive program and their potential role in the same. Internationally, allied health personnel have played central roles in coordination and execution of ECMO runs.

Limitations

Most international literature is centered on allied health models around nurse practitioners hence not much literature on PAs as ECMO specialists available. In absence of any data, this document is more of a proposal rather than a review.

Further research on possible PA Education for ECMO and MCS and programs using PAs as cannulation, retrieval and coordinator roles are needed.

Conclusion

ECMO services are now full-fledged programs requiring a myriad of health care professionals. Multidisciplinary teams that include PAs can improve program quality from initiation, cannulation management to decannulation. Because of their multifaceted training, PAs are well placed in the Indian healthcare system to be ECMO specialists leading in program implementation. The starting point would be to introduce PAs to ECMO education through workshops, simulations, and include ECMO training in the PA curriculum. With the increasing use of ECMO in various critical care set ups, it would open up a whole new career options for PAs.

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Immunization System Resilience and Measles Outbreak Prevention: A Narrative Review of India and Bangladesh

Monika Kochar

Abstract

Importance: Bangladesh reported a rapid rise in measles cases in Q1 2026, with 676 confirmed infections and more than 38 reported child deaths by March 2026, and a quarterly incidence of 3.9 cases per million. If sustained for a full year, this quarterly rate would correspond to an annualized incidence of approximately 15.6 cases per million, above India's highest post-COVID-19 annual incidence of 10.4 cases per million in 2023. This outbreak occurred despite Bangladesh's historical participation in World Health Organization (WHO)-supported immunization programs, raising questions about the structural determinants of program resilience. This review compares selected programmatic, logistical, and governance features of the immunization systems of India and Bangladesh, with a focus on factors relevant to measles prevention and program resilience.

Observations: A narrative review with a comparative health systems perspective was conducted using WHO Global Health Observatory case data, WHO/United Nations Children's Fund (UNICEF) estimates of national immunization coverage (WUENIC) for 2019–2023, Bangladesh surveillance and program reports, India's Health Management Information System (HMIS) data for 2024–2025, official program documents, and relevant peer-reviewed literature. Incidence rates were calculated using reported case totals and United Nations Population Division population estimates. Because coverage data are asymmetric, Bangladesh WUENIC estimates are presented as low-confidence modeled estimates and are not used for quantitative comparison with India. Analysis was structured around 4 domains of immunization system resilience: institutional continuity, subnational outreach, supply chain management, and supplementary immunization activity (SIA) calendar maintenance. India's measles-containing vaccine, dose 1 (MCV-1) coverage reached 97.8% in 2024–2025 after a post-COVID-19 dip to 85% in 2020, with measles incidence declining 73% year-on-year. Bangladesh's WUENIC coverage estimates are low-confidence extrapolated values, while the 2026 outbreak provides evidence of substantial immunity gaps. Four structural factors distinguish India's approach: (1) institutional continuity of the Universal Immunization Programme since 1985; (2) targeted subnational outreach through Mission Indradhanush, reaching 54.6 million missed children; (3) real-time supply chain monitoring via eVIN (Electronic Vaccine Intelligence Network) and U-WIN (Universal Immunization WIN); and (4) a maintained SIA calendar, contrasting with Bangladesh's canceled 2024 campaign.

Conclusions and Relevance: The narrative comparison suggests that immunization system resilience depends on sustained institutional continuity, targeted outreach, reliable logistics and supply chain systems, and timely SIAs. Bangladesh's Q1 2026 observed incidence was 3.9 cases per million; an annualized projection of approximately 15.6 cases per million would exceed India's highest post-COVID-19 annual incidence of 10.4 cases per million, but the projection should not be treated as an observed annual rate. The findings highlight the importance of examining subnational immunity gaps and program functioning alongside national coverage estimates when assessing measles programme resilience.

Keywords Measles, incidence per million, immunization system resilience, Universal Immunization Programme, Mission Indradhanush, eVIN, Bangladesh outbreak, WUENIC data quality, vaccine-preventable disease, India

Introduction

Measles remains a leading cause of vaccine-preventable child mortality globally. Despite the availability of a safe and

effective 2-dose vaccine regimen for more than 6 decades, the disease reemerges recurrently wherever immunization coverage falls below the herd immunity threshold of 95%.¹ Measles has a basic reproduction number (R_0) of 12 to 18, meaning a single infectious case generates up to 18 secondary infections in a fully susceptible population. This exceptional transmissibility means that even modest coverage shortfalls, sustained over several years, can generate the susceptible cohort necessary for explosive outbreak-level transmission.²

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In early 2026, Bangladesh reported a rapidly escalating measles outbreak that illustrates how accumulated immunity gaps can contribute to epidemic transmission. The Bangladesh outbreak was reported with 676 confirmed cases and more than 38 reported child deaths by March 2026.³ The Q1 2026 incidence was approximately 3.9 cases per million population, producing an annualized projection of approximately 15.6 cases per million if the quarterly rate were sustained.³ The outbreak disproportionately affected young children, including infants under 9 months, consistent with substantial immunity gaps among older children and recent birth cohorts.³

India, which shares a lengthy border with Bangladesh and presents broadly comparable challenges of population scale, geographic heterogeneity, and health system complexity, did not experience a comparable resurgence over the same period. India's measles incidence, which had reached 10.4 cases per million in 2023, continued the downward trajectory documented through 2021⁴ and declined further in 2024, consistent with a 73% reduction in reported cases recorded by India's Health Management Information System (HMIS).⁵

The incidence comparison provides useful context, but the observed rates should be interpreted with the limitations of surveillance and reporting in mind. India's highest post-COVID-19 annual incidence was 10.4 cases per million in 2023, whereas Bangladesh recorded 3.9 cases per million in Q1 2026. Only the hypothetical annualized Bangladesh rate of approximately 15.6 cases per million would exceed India's 2023 annual rate. The comparison is therefore used to contextualize reported burden rather than to establish a causal difference in system performance. This narrative review examines selected structural, logistical, and programmatic features that may be relevant to the observed divergence.

Methods

This narrative review compares selected features of the immunization systems of India and Bangladesh, with a comparative health systems perspective focused on institutional continuity, sub-national outreach, supply chain management, and supplementary immunization activities (SIAs). The countries were selected because of geographic proximity, shared epidemiologic experience with measles, and broadly comparable challenges related to population scale and health system delivery. The comparison is descriptive rather than causal, and it does not assume that shared contextual features eliminate confounding. Because the underlying data are not symmetrically comparable, the review should be read as a structured comparison of system features rather than a matched quantitative or causal analysis.

The primary epidemiologic metric used for contextual comparison is measles incidence expressed as cases per million population per year, or per quarter where annual data are

not yet available. This metric was chosen instead of absolute case counts because of the substantial population difference between India (approximately 1.43 billion) and Bangladesh (approximately 174 million). Incidence rates were calculated from World Health Organization (WHO) Global Health Observatory (GHO) annual reported case totals divided by United Nations Population Division midyear population estimates for the corresponding year and country.^{6,7} For Q1 2026, Bangladesh rates were calculated from reported totals divided by the 2026 estimated population.

Coverage data were drawn from WHO/United Nations Children's Fund (UNICEF) estimates of national immunization coverage (WUENIC) for the period 2019–2023 and from India's HMIS for 2024–2025. A critical methodological caveat applies to Bangladesh WUENIC estimates: WHO/UNICEF excluded all nationally reported administrative coverage data for Bangladesh in this period because reported values systematically exceeded 100% and were judged unreliable. All published WUENIC coverage figures for Bangladesh (MCV-1 [measles-containing vaccine, dose 1]: 97%; MCV-2 [measles-containing vaccine, dose 2]: 93%, 2019–2023) are therefore extrapolated estimates carrying the lowest WHO Grade of Confidence.⁸ These figures are presented to describe the available evidence but should not be interpreted as verified field coverage.

Because of this data-quality asymmetry, India and Bangladesh are not treated as equivalent quantitative cases. India's coverage data for 2019–2023 are drawn from WUENIC, while HMIS data are used for 2024–2025. Bangladesh's WUENIC figures are modeled extrapolations with no independently verifiable field data and are not used to calculate comparative percentage point gaps against India. Measles incidence is used only to provide contextual comparison of reported burden, with the same limitations regarding surveillance sensitivity applying to both countries. In the absence of reliable Bangladesh coverage data, the 2026 outbreak provides important evidence that substantial immunity gaps persisted, but it does not directly measure the proportion of the population that is immune.

Program documentation reviewed included Universal Immunization Programme (UIP) operational guidelines and budget data, Mission Indradhanush (MI) program reports, eVIN and U-WIN (Universal Immunization WIN) technical documentation from the United Nations Development Programme (UNDP) and Ministry of Health and Family Welfare (MoHFW), and Directorate General of Health Services Bangladesh press briefings from March to April 2026. Peer-reviewed literature was identified through PubMed and Google Scholar using the terms “measles India incidence,” “immunisation system resilience,” “vaccine supply chain,” and “catch-up vaccination.” The review was structured around 4 hypothesized domains of immunization system resilience: (1) institutional continuity, (2) subnational

outreach capacity, (3) supply chain and logistics management, and (4) SIA calendar maintenance.

Results

Epidemiologic Context

The Table summarizes selected immunization system features relevant to measles prevention in India and Bangladesh. Because comparable quantitative program indicators are not consistently available for both countries, the table focuses on system domains rather than attempting to combine coverage, incidence, mortality, data-quality caveats, and interpretation in a single quantitative table. India's MCV-1 coverage, reported through the HMIS for 2024–2025, reached 97.8%; earlier 2019–2023 coverage estimates are from the WUENIC. No equivalent quantitative coverage gap is calculated for Bangladesh because its WUENIC estimates are modeled extrapolations rather than field measurements.

Domain 1: Institutional Continuity of the Immunization Program

India's UIP was launched in 1985, building on the Expanded Programme on Immunization (EPI) established in 1978, and has been structurally embedded within the National Health Mission since 2005.^{9,10} It currently covers 12 vaccine-preventable diseases, reaches an estimated 29 million pregnant women and 26 million newborns annually, and is funded entirely by central government allocations at a budget of approximately INR 72.34 billion (US \$860 million) in 2022.¹¹ All vaccines are provided free of cost to residents, including noncitizens. The program's 40-year institutional continuity has proven robust to political transitions, fiscal pressures, and external shocks. India eradicated polio in 2014 and eliminated maternal and neonatal tetanus in 2015 through the same delivery infrastructure.¹² Critically, MCV-1 coverage recovered from its COVID-19 low of 85% (2020) to 95% by 2022 and 97.8% by 2024–2025, demonstrating the program's capacity for rapid self-correction.¹³

Table Key Immunization System Features Relevant to Measles Prevention in India and Bangladesh^a

Domain	India	Bangladesh	Comparative point
Program continuity	UIP since 1985; integrated with the National Health Mission	EPI since the late 1970s; recent disruptions to routine immunization and supplementary activities reported	Continuity of routine program functions is important during administrative or political disruption
Subnational outreach	Mission Indradhanush targets zero-dose and underimmunized children	The 2026 outbreak indicates persistent susceptible groups; comparable nationwide tracking data are limited	National averages may conceal local immunity gaps
Supply chain systems	eVIN supports vaccine stock and cold chain monitoring	Reported disruptions to immunization activities highlight operational vulnerabilities	Operational resilience depends on reliable supply chain and readiness monitoring
Beneficiary tracking	U-WIN supports individual vaccination records and dose tracking	Comparable nationwide digital beneficiary tracking information was not identified in the sources reviewed	Individual tracking may help identify missed doses
Supplementary immunization	Large MR campaigns and subsequent elimination-focused activities have been conducted	Major MR SIA in 2020; WHO reports no regular nationwide supplementary MR campaigns since then	Catch-up activities may reduce accumulation of susceptible cohorts
Measles burden/immunity gaps	Post-COVID-19 resurgence followed by decline; subnational gaps remain	Major outbreak in 2026 demonstrated substantial immunity gaps	Outbreaks indicate susceptibility but do not directly quantify national population immunity
Residual challenges	Coverage heterogeneity, hesitancy, migrant tracking, and zero-dose children	Immunity gaps, program continuity, supply/logistics, and timely catch-up	Both programs retain vulnerabilities requiring continued surveillance and targeted action

Abbreviations: EPI, Expanded Programme on Immunization; eVIN, Electronic Vaccine Intelligence Network; MoHFW, Ministry of Health and Family Welfare; MR, measles-rubella; SIA, supplementary immunization activity; UIP, Universal Immunization Programme; UNDP, United Nations Development Programme; U-WIN, Universal Immunization WIN; WHO, World Health Organization.

^aSources: Program, surveillance, and immunization system documents cited in the Results subsections on institutional continuity, subnational outreach, supply chain management, and SIA calendar maintenance, including WHO/UNICEF, Government of India/MoHFW, UNDP, and Bangladesh outbreak and program sources.

Bangladesh's EPI, initiated in the late 1970s, was historically effective and internationally recognized. However, the 2026 outbreak highlights vulnerabilities associated with disruptions to routine immunization and catch-up activities. UNICEF and WHO reported disruptions in measles-containing vaccine coverage during 2024–2025 and the absence of regular nationwide supplementary measles-rubella (MR) campaigns since 2020.³ These disruptions may have contributed to the accumulation of susceptible cohorts. The comparison therefore suggests that continuity of routine program functions and the ability to maintain catch-up activities during periods of disruption are important components of immunization system resilience.

Domain 2: Subnational Outreach and Zero-Dose Reduction

National coverage averages mask subnational heterogeneity that can sustain localized transmission chains. In India, MI, launched in 2014 and intensified through multiple phases from 2017 onward, was specifically designed to address residual pockets of undervaccination.¹⁴ Districts identify zero-dose and underdosed children by name and household, then deploy targeted campaign sessions in remote tribal regions, urban informal settlements, and migrant communities. Since launch, MI and its phases have immunized 54.6 million children and 13.2 million pregnant women not reached through routine services.¹⁵ India's reported zero-dose rate was 0.06% of the total population in 2024.¹⁶ The Zero-Dose Implementation Plan 2024 further targets 143 high-burden districts in 11 states with residual gaps.¹⁷

The 2026 Bangladesh outbreak disproportionately affected young children, including infants younger than 9 months.³ This age distribution is consistent with substantial immunity gaps and transmission among susceptible groups. The comparison highlights the value of subnational and individual-level tracking for identifying missed or underimmunized populations before they become visible through outbreak transmission.

Domain 3: Supply Chain and Logistics Management

Bangladesh experienced reported disruptions to routine immunization and vaccination activities during the period preceding the 2026 outbreak.³ This illustrates an operational vulnerability that may not be captured adequately by aggregate coverage estimates alone. Reliable monitoring of vaccine availability, cold chain performance, consumables, and campaign readiness can help programs identify operational gaps before they affect planned vaccination activities.

India has systematically addressed this class of vulnerability through the Electronic Vaccine Intelligence Network (eVIN), developed with UNDP support and operational since 2015. eVIN provides real-time stock and cold chain performance data across the entire distribution hierarchy, from national to facility level, with automated prestockout alerts enabling preemptive redistribution.¹⁸ U-WIN, launched nationally in 2024, extends this digital infrastructure to the individual beneficiary level: the platform creates vaccination records for every child from birth to age 16 years, linked to Aadhaar, and generates automated appointment reminders for due doses.¹⁹ Together, these systems can complement aggregate coverage estimates with timely operational and beneficiary-level information. eVIN has also been adapted as a model system in Indonesia, Malawi, and Sudan.²⁰

Domain 4: SIA Calendar Maintenance

Even at 95% routine coverage, unvaccinated children accumulate annually into a susceptible cohort capable of sustaining outbreak-level transmission within 3 to 5 years. Periodic SIAs that sweep across multiple birth cohorts are therefore a structural requirement of measles elimination, not an optional addition to routine programs.²¹ Critically, an irregular SIA schedule is worse than a consistently maintained one, because it generates false assurance while immunity debt accumulates silently.

India conducted a nationwide MR SIA in 2017–2019, cumulatively vaccinating over 348 million children aged 9 months to 15 years across the country by 2023,²² followed by the National Zero Measles-Rubella Elimination Campaign, launched on April 24, 2025.²³ Bangladesh conducted its most recent major MR SIA in 2020, and WHO reported an absence of regular nationwide supplementary MR campaigns since then.³ In the context of disruptions to routine immunization, this gap may have contributed to the accumulation of susceptible cohorts, although the available evidence does not permit a causal attribution.

Discussion

The narrative comparison suggests that incidence per million provides useful context for understanding the reported measles burden, while also requiring careful interpretation because surveillance sensitivity and data completeness may differ. India's annual incidence reached 9.1 to 10.4 cases per million during its worst post-COVID-19 years (2022–2023).^{24,25} Bangladesh's Q1 2026 incidence was 3.9 cases per million in the observed quarter, with an annualized projection of approximately 15.6 per million if the quarterly rate were sustained. The observed quarterly rate therefore did not itself

exceed India's 2023 annual rate; only the hypothetical annualized projection did.

The epidemiological literature identifies declining routine coverage, accumulation of susceptible cohorts, and gaps in timely supplementary immunization as important contributors to measles resurgence.²⁶⁻²⁸ In Bangladesh, the available evidence points to immunity gaps and disruptions in routine immunization and supplementary activities.³ The country's WUENIC-reported MCV-1 coverage of 97% is a low-confidence extrapolated estimate rather than a verified field measurement.⁸ The 2026 outbreak therefore demonstrates substantial immunity gaps and raises questions about whether the national estimate adequately reflected subnational coverage. It should not be interpreted as proof that the reported 97% estimate was impossible or that the outbreak directly measured population immunity.

A second important finding highlighted by the comparison is the role of supply chain and operational digitization as a risk-mitigation layer. Bangladesh's reported disruptions to immunization activities illustrate how operational constraints may affect program delivery without being fully visible in aggregate coverage estimates. India's eVIN architecture provides a mechanism for converting stock and cold chain information into actionable operational signals before shortages or interruptions affect service delivery.¹⁸ Its value therefore extends beyond efficiency to support program continuity and readiness.

More broadly, the comparison suggests that immunization program resilience benefits from arrangements that can continue functioning during political or administrative disruption. India's UIP has been maintained across multiple government transitions over 4 decades and is supported by state, district, block, and village-level health workers, including the Accredited Social Health Activist (ASHA) network. This operational depth may contribute to continuity during periods of disruption. Bangladesh's 2026 experience highlights the importance of maintaining routine immunization and catch-up functions during periods of administrative or operational stress.

Limitations

This narrative comparison carries several important limitations. First, the 2-country comparison cannot establish causation, and the asymmetry between India's available HMIS/WUENIC data and Bangladesh's low-confidence WUENIC extrapolations means the 2 cases cannot be compared on fully equivalent evidentiary terms. The review is accordingly structured as a qualitative comparison of system features across 4 resilience domains rather than a matched quantitative or causal analysis. Unmeasured contextual differences, including population density, nutritional status, healthcare access, and surveillance sensitivity, may also contribute to the observed

divergence in reported outcomes. Second, Bangladesh's 2026 epidemiological data are preliminary and subject to revision as case-based surveillance is completed. Third, India's HMIS coverage data are administrative estimates that may be subject to denominator inconsistencies in some states. Fourth, the incidence calculations for India rely on WHO GHO reported case totals, which are acknowledged to underestimate true incidence due to incomplete case detection and reporting.²⁹ The same reporting sensitivity caveat applies to Bangladesh. Comparative incidence figures should therefore be read as indicators of relative system performance rather than as precise epidemiologic estimates. Fifth, the evidentiary depth available for the 4 resilience domains is itself asymmetric: richer, more granular programmatic data exist for India (eg, ASHA workforce figures, eVIN coverage, SIA campaign statistics) than for Bangladesh, where equivalent operational detail is not publicly available. Readers should weigh the domain-by-domain comparisons accordingly, treating India-side evidence as more granular description and Bangladesh-side evidence as necessarily more inferential.

Residual Vulnerabilities in India's Program

Vaccine hesitancy, amplified through social media, has been associated with localized measles clusters in 2022–2024 and is an increasing concern in several states.²⁹ Migrant populations who move between states for seasonal work frequently fall between origin and destination tracking systems, creating a structurally invisible cohort of undervaccinated individuals.³⁰ Subnational coverage heterogeneity also remains significant, and districts in Uttar Pradesh, Bihar, Rajasthan, and several northeastern states continue to report MCV-1 coverage below 95%.¹⁷ India's own 2022–2023 incidence spike to 9.1–10.4 cases per million, although subsequently controlled, demonstrates that the system remains vulnerable to post-COVID-19 catch-up dynamics and persistent subnational susceptibility.

Conclusions

This narrative review highlights 4 immunization system features that appear relevant to resilience in the India-Bangladesh comparison: long-term institutional continuity of the immunization program; targeted subnational outreach to zero-dose and hard-to-reach populations; real-time digital supply chain and beneficiary tracking; and maintenance of a regular SIA calendar. The comparison suggests that India's reported per capita case burden has remained lower than Bangladesh's 2026 trajectory, while recognizing that Bangladesh's 3.9 cases per million in Q1 2026 was an observed quarterly rate and that approximately 15.6 per million is only an annualized projection if the quarterly rate were sustained.

The Bangladesh case also illustrates a methodologic lesson for immunization surveillance: WUENIC estimates that lack direct empirical support and carry low WHO Grades of Confidence should be interpreted cautiously and should not be treated as definitive evidence of program adequacy. National coverage estimates may coexist with important subnational immunity gaps, and outbreak surveillance can provide important evidence that susceptibility persists even when national estimates appear high.

These India-Bangladesh findings arise from a 2-country narrative comparison with asymmetric underlying data and cannot, on their own, be generalized to low- and middle-income countries as a class. With that scope condition stated, the comparison provides a useful basis for policy discussion: it suggests that coverage metrics alone may be insufficient proxies for program resilience, and that supply chain monitoring system adequacy, SIA calendar regularity, continuity of routine program operations, and subnational coverage heterogeneity are plausible additional indicators for further study across a larger set of country cases. India's approach illustrates one workable, if imperfect, model rather than a validated template; its own continued success depends on closing remaining district-level gaps, addressing vaccine hesitancy, and extending individual beneficiary tracking to migrant populations, and its transferability to other health systems remains an open empirical question beyond the scope of this analysis.

Generative AI Use

The authors used generative AI tools (Grammarly and QuillBot) to assist with grammar correction and language refinement during manuscript preparation. All content was reviewed and approved by the author.

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Minimally Invasive Redo Mitral Valve Replacement After Prior Annuloplasty Ring Repair

Satyajit Patra, Binay Krishna Sarkar, Mondira Mondal, Biswajit Mondal

Abstract

Redo mitral valve surgery after failed annuloplasty is technically challenging, particularly because of adhesions encountered during repeat sternotomy. A minimally invasive right minithoracotomy with peripheral cannulation provides an alternative method to mitigate these risks. This report concerns a 33-year-old woman who initially underwent mitral valve surgery with a Carpentier-Edwards (CE) annuloplasty ring. She was later admitted with severe respiratory distress and fatigue. Preoperative evaluation revealed moderate mitral regurgitation, borderline transmitral gradients, and preserved ventricular function. Redo mitral valve replacement was performed via right minithoracotomy with peripheral (femoro-femoral) cardiopulmonary bypass (CPB). During the intervention, the implanted annuloplasty ring appeared distorted and leaflet motion was restricted. A 27-mm bioprosthetic valve was implanted using a total chordal-preserving technique. The heart gained sinus rhythm immediately after removal of the cross-clamp without complications. She was weaned from ventilation within 6 hours, remained in the intensive care unit (ICU) for a brief period, and was discharged on the fifth postoperative day (POD). At 6-month follow-up, she showed good functional recovery and normal prosthetic valve function and was asymptomatic. This report demonstrates that redo minimally invasive mitral valve replacement with peripheral cannulation and preservation of the subvalvular apparatus is feasible in a young patient after failed repair. Furthermore, it highlights the challenges encountered when selecting among options, such as choosing a prosthesis for younger patients. These highly detailed procedural insights expand the existing literature by facilitating the safe application of minimally invasive techniques even in complex redo cases.

Keywords Redo mitral valve surgery, minimally invasive cardiac surgery, mitral valve replacement, annuloplasty failure, chordal preservation

Introduction

Mitral valve replacement remains the most effective treatment for degenerative mitral regurgitation as initially described by Carpentier.¹ Mitral valve repair, however, has the advantage of maintaining the valve's function locally as well as the geometry of the left ventricle, which results in better long-term survival and fewer complications, such as thromboembolism in patients, compared with valve replacement.¹ In one

reoperation series, the main reasons for the failure of repair were leaflet prolapse and progressive degeneration.²

One of the factors that generally makes mitral reoperative surgery quite challenging is that the standard approach is repeat sternotomy. This approach is usually associated with the presence of tight mediastinal adhesions, and the risk of injury to cardiac structures or the aorta is quite high.^{3,4} Approximately 7% of cardiac reoperations were complicated by adverse events, such as graft or cardiac injury, mainly at the time of sternal reentry.⁴ Such accidents contribute to the increased incidence of stroke and mortality.⁵ For many years, minimally invasive mitral valve replacement surgery, via right minithoracotomy with peripheral cannulation, has been used for both primary and redo cases.³ In this way, the sternum is neither divided nor are anterior adhesions dissected.³ The latest research shows that performing mitral valve replacement surgery through minithoracotomy has the same safety and efficacy as conventional surgery, but with complications and percentages of mortality being very low and replacement success being very high.^{3,6} Compared with sternotomy,

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minimally invasive mitral valve replacement surgery is generally associated with less time on ventilation, less blood loss, fewer transfusions, and shorter ICU and hospital stays.^{6,7}

The right minithoracotomy approach for redo mitral surgery has more than a decade of supporting evidence.³ Therefore, case reports in this setting should focus on specific clinical lessons. The uniqueness of this case lies in: (1) the combination of minimally invasive cardiac surgery and peripheral cannulation for total chordal-preserving mitral valve replacement in a redo scenario after annuloplasty failure, (2) decision-making tailored to a young patient with mixed mitral pathology, and (3) highlighting the technical and clinical dilemmas. Here, we narrate the perioperative course and surgical techniques in detail. The objective of this study is to discuss critical technical points, such as patient positioning, cannulation method, and myocardial protection; establish the outcomes of redo minimally invasive mitral surgery; and present the current literature.

Case Presentation

A 33-year-old woman presented with progressively worsening shortness of breath on exertion over several months, with New York Heart Association (NYHA) functional class III. In addition, she frequently experienced palpitations, chest pain, and shortness of breath. Her medical history showed that she had atrial fibrillation (AF) and an embolic stroke that left her with right-sided hemiparesis a year ago. On February 18, 2014, the patient underwent mitral valve repair for degenerative regurgitation with a 28-mm CE Classic annuloplasty ring via median sternotomy with central cannulation. The postoperative period was uneventful. The patient was discharged on POD 6 and was prescribed acenocoumarol for AF.

After mitral valve repair with a ring, the patient's symptoms did not improve. Transthoracic echocardiography revealed severe mitral regurgitation, increased transmitral gradients, and a markedly enlarged left atrium with AF. The indication for mitral valve replacement is severe valve pathology that cannot be managed with rerepair. Therefore, mitral valve replacement was performed. Preoperative Doppler imaging was obtained. Based on these findings, she was considered a suitable candidate for minimally invasive right thoracotomy.

Surgical Technique

Under one-lung ventilation and anesthesia, the patient was positioned supine with the right side of the chest elevated approximately 30° and the right arm fixed alongside the body. Two external defibrillator pads were fixed. Transesophageal echocardiography (TEE) was used throughout the operation. A 6-cm incision was made in the right anterolateral

thoracotomy in the fourth intercostal space. Cannulation was performed peripherally by first cannulating the right femoral artery and vein through a groin incision. Prolene stay sutures (6-0 polypropylene) were prepared, and silk ties with vessel loops were used to control the proximal and distal segments. After systemic heparinization (300 or 400 IU/kg with an activated clotting time ≥ 480 s), femoral arterial cannulation was attempted with the modified Seldinger technique under direct visualization. After a guidewire was inserted and its position was confirmed inside the lumen, a 20 Fr arterial cannula was inserted. A guidewire was used, and under the guidance of TEE, a 23 Fr venous cannula was threaded to the junction of the inferior vena cava and right atrium, following femoral venous cannulation, which was performed with a 6-0 polypropylene purse-string suture. In addition, to facilitate venous drainage, a 16 Fr right internal jugular venous cannula was inserted under ultrasound guidance with the Seldinger technique. To allow antegrade limb perfusion, a 5 Fr distal perfusion cannula was placed in the femoral artery.

The important surgical steps are as follows:

1. CPB was set up with femoral cannulation, and the patient's body temperature was gradually lowered to 28°C.
2. A transthoracic Chitwood cross-clamp was applied to the ascending aorta through a separate small incision in the second intercostal space.
3. Antegrade cardioplegia (Del Nido) was administered via a cardioplegia cannula.
4. Carbon dioxide was introduced into the chest at a rate of 1 L/min throughout the operation to reduce the risk of left ventricular air embolism.
5. A left atrial vent was inserted through the right superior pulmonary vein for the perfect and continuous decompression of the left side of the heart, as well as an efficient means of deairing, especially in cases of minimally invasive mitral valve surgeries (MIMVSS) where exposure is limited. In addition to the aforementioned functions, the vent also acted as a tool to keep the operating field clear and ensure that all intracardiac air was removed.
6. A left atriotomy was performed through Sondergaard's groove to expose the left atrium. After incising, the previous annuloplasty ring was identified. Fibrosis was noted in the annulus, but the tissue did not show signs of endocarditis or evidence of vegetation. The native leaflets were thin and free of perforations or flail segments, but their motion was limited by rigid rings and scar tissue.
7. Valve excision and implantation: After the old ring (Figure 1) was removed, all mitral valve leaflet tissues were removed except for a small fragment of the posterior leaflet. The mitral valve was replaced with multiple interrupted, pledgeted 2-0 braided polyester (Ethibond) sutures inserted circumferentially in a supra-annular position using a total chordal-preserving technique to maintain the original

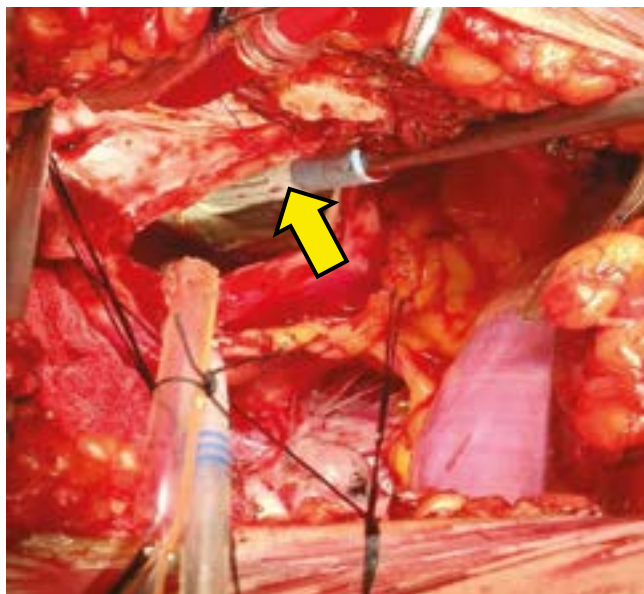


Figure 1 Intraoperative view showing exposure of the left atrium and previously repaired mitral valve ring in situ

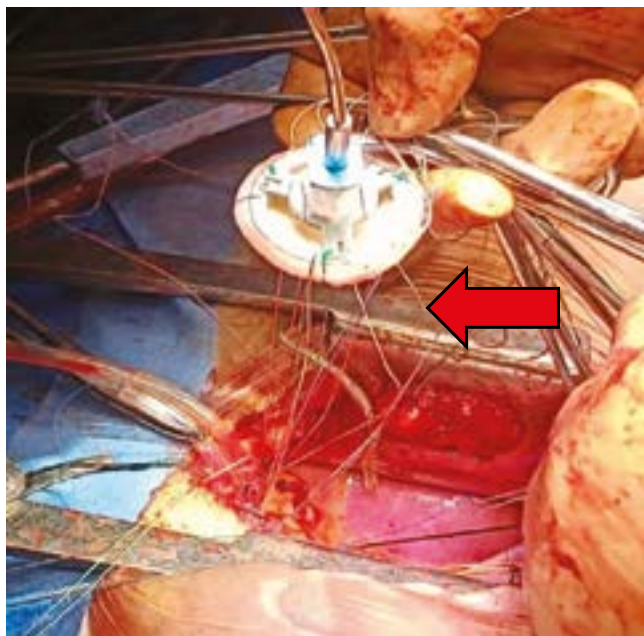


Figure 2 Prosthetic valve placement in progress with multiple sutures applied circumferentially for fixation

left ventricular shape (Figure 2). A 27-mm porcine stented bioprosthetic valve was implanted. A left atrial maze procedure was performed simultaneously for AF.

8. The final stage of deairing involved shutting off the suction from the left atrial vent periodically to allow sufficient filling of the heart until TEE verified the absence of air and complete filling of the left ventricle. When CPB was gradually stopped, protamine was administered to

reverse the heparin effect. CPB and cross-clamp times were 200 and 102 min, respectively. Intraoperative TEE revealed that the bioprosthetic mitral valve was well positioned and had no paravalvular leak with a mean gradient of 4 mm Hg. We used a regional intercostal block using USG Doppler.

Postoperative Outcome

After surgery, the patient was removed from the ventilator 10 h after surgery, and the heart rhythm was in normal sinus rhythm. Echocardiography performed on POD 1 showed that the bioprosthetic mitral valve function was normal with no mitral regurgitation. The left ventricle was still functioning well, with an ejection fraction of 60%. The recovery was uneventful. At 3-month follow-up, the patient remained asymptomatic and in sinus rhythm with a competent echocardiographic valve prosthesis.

Discussion

This case highlights key issues associated with redo mitral valve surgery.

First, it reveals that mitral valve replacement may be required even after initial mitral valve repair in young patients.¹ Typically, Carpentier's "French correction," ie, mitral valve repair, is preferred for treating degenerative mitral valve disease. However, in a few cases, the repair may eventually fail. Some valve failure mechanisms include leaflet degeneration (myxomatous change), annulus dilatation, and obstruction by the ring. Our patient had persistent AF, and her history of rheumatic heart disease may have caused annular fibrosis and recurrent mitral regurgitation. As the ring was very stiff and symptoms persisted, reoperation was not considered a viable option, and we decided on valve replacement surgery.

Second, implantation of a bioprosthetic valve in a 33-year-old woman raises several issues that require thorough and careful discussion with the patient. Mechanical prostheses can last longer and are generally preferred for younger patients; however, these devices require lifelong anticoagulation with drugs such as warfarin or acenocoumarol. For women of childbearing age, planning a pregnancy, or already pregnant, the use of warfarin is problematic because of its high teratogenic risk and major difficulties in managing the patient postdelivery.⁸ Although postoperative AF persisted in this case, the 2024 European Society of Cardiology/European Association for Cardio-Thoracic Surgery (ESC/EACTS) guidelines for AF recommend a regimen for vitamin K antagonists that has a much lower intensity. The guidelines target an international normalized ratio of 2.0 to 3.0, whereas mechanical prostheses require a higher intensity of anticoagulation therapy. Thus,

there is a lower risk if we give the patient the option of future pregnancy, allowing her to remain on the lowest dose of medication, which makes it a safer choice. In addition, the patient had a history of stroke and AF and was not keen to adopt a strong anticoagulant regimen unless it was absolutely necessary, in line with our discussion. After counselling, the patient decided on a tissue valve. They understood it would likely need to be replaced within 10 to 15 years. But chordal preservation helps maintain annuloventricular continuity, giving a near-native functional outcome.¹

Third, the main benefits of the minimally invasive right thoracotomy approach were as follows:

1. No re sternotomy: Saving patients from re sternotomy also helps avoid the problems of reopening dense anterior sticking layers and sternal wires, which are associated with major bleeding more frequently in case of redo operations.^{2,3}
2. Peripheral cannulation only: CPB was performed via peripheral femoro-femoral cannulation (Figure 3). TEE was used to assess the condition of the mitral valve during the procedure and to examine the function of the prosthetic valve after valve replacement. In addition, topical hypothermia, in which cold saline was dripped on the heart, was performed to further enhance myocardial protection.
3. Incision and exposure: Via a right minithoracotomy in the fourth intercostal space (~6 cm), excellent visualization of the mitral valve was obtained through a left atrial approach.
4. Myocardial protection: Most myocardial protection factors work together to protect the myocardium. Systemic hypothermia was performed at 28°C, combined with topical cooling with cold saline drips, and antegrade blood

cardioplegia was administered via the aortic root. After aortic cross-clamp removal, coronary perfusion and sinus rhythm were restored. CO₂ insufflation at 1 L/min effectively deaired the field, which is the standard approach in MIMVS to prevent neuroembolic events.

5. Deairing and weaning: Deairing was performed using the left atrial vent inserted through the right superior pulmonary vein, and left heart decompression was performed. Once the aortic cross-clamp was removed, deairing was performed via aortic root suction through the cardioplegia cannula (root reverse technique) and controlled left atrial venting, with intermittent clamping of suction to allow adequate cardiac filling. Using TEE, it was verified that no air was trapped in the ventricle before the patient was removed from the bypass machine. The positive outcomes of MIMVS documented in the literature reflect our clinical experience.

Research has shown that patients undergoing MIMVS have significant advantages over those undergoing conventional sternotomy. These advantages include reduced mechanical ventilation time, bleeding, blood transfusion, and length of ICU and hospital stay.⁴ For example, a large study of 1604 patients, among whom 13.6% were redo cases, found that MIMVS had a very low hospital mortality rate of only 1.1% and an overall survival rate at 10 years of 88%. Conversion to sternotomy was rare (2%), indicating that the method is feasible even for reoperations.⁶ Prolonged intubation for 12 hours, 1 day in the ICU, and discharge on POD 5 are factors of rapid recovery, to which our patient's outcome fits very well.^{4,5} However, some authors suspect that the minimally invasive approach itself causes chest wall adhesions at the thoracotomy site, which may complicate future surgeries.³ Indeed, any previous incisions will always lead to scar tissue, but the argument is that a right thoracotomy scar creates fewer problems than a re-entered sternotomy scar.² In our operation, we used a right-sided chest incision as an alternative surgical plane to avoid dense anterior mediastinal adhesions from the first operation.

Limitations and Alternatives

Use of minimally invasive techniques for redo mitral surgery has been extensively documented.² Due to the annotated pictures released with the study, this case will be of great value, especially to junior surgeons who will learn the step-by-step surgical decision-making in a very young patient with late failed mitral annuloplasty and combined mitral pathology at presentation. In patients at extremely high surgical risk, alternative approaches, such as transcatheter mitral valve-in-ring or valve-in-valve procedures, can be considered. However, for relatively young and fit patients, this option remains effective and durable.



Figure 3 Postoperative wound showing healed surgical incision with sutured site and surrounding skin changes. A, Previous median sternotomy scar. B, Peripheral cannulation for cardiopulmonary bypass (CPB). C, Minimal right chest incision for redo mitral valve replacement

Patient Selection

Our last sentence in the text mentions “suitable for certain patient groups,” and here it focuses on the selection of patients for whom peripheral cannulation would not only be feasible but also accompanied by the right anatomical factors.⁹ Specifically, these patients should have no severe aortic calcification, femoral vessels of adequate size, and no significant lung adhesions. Assessment of these factors requires preoperative imaging techniques such as echocardiography, ultrasound, and computed tomographic angiography (in some cases).¹⁰ We also consider body habitus because MIMVS can be extremely challenging in obese patients. Briefly, our patient selection process, similar to that of many other centers, involved multidisciplinary case review and imaging workup.⁹

Conclusion

A right minithoracotomy allows safe redo mitral valve replacement after a failed repair, thereby avoiding the need for repeat sternotomy. In this patient with peripheral cannulation, mitral valve replacement via a minimally invasive approach yielded excellent outcomes without perioperative complications. According to published data, minimally invasive redo mitral surgery is associated with low mortality and morbidity rates and allows for faster patient recovery.^{2,5}

Success relies on appropriate patient selection through preoperative imaging and surgeon expertise in peripheral cannulation, cardioplegia delivery, and thorough deairing, as previously described. We believe that this case illustrates the potential of current minimally invasive techniques to expand the surgical options for patients with complex valvular diseases. These findings are consistent with contemporary evidence demonstrating that minimally invasive redo mitral valve surgery via right minithoracotomy is a safe and effective alternative to conventional sternotomy, offering reduced perioperative morbidity and faster recovery in appropriately selected patients.^{6,7}

Ethics Approval

This report describes treatment and follow-up of a single patient receiving routine clinical care at NRS Medical

College, Kolkata. In accordance with institutional policy, the Institutional Ethics Committee (IEC) does not issue written approval for single case reports because they are not considered human research and therefore do not require retrospective ethics review. This practice is consistent with Committee on Publication Ethics (COPE) guidance stating that dissemination of an individual case arising from routine care is not research and does not require ethics review, unlike randomized trials or large clinical series. Written informed consent for publication of case details and images was obtained from the patient, who reviewed the manuscript prior to submission.

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