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Risk factors associated with saphenous vein graft aneurysm after coronary artery bypass graft

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Introduction: Saphenous vein graft aneurysm (SVGA) is a rare but life-threatening complication following coronary artery bypass grafting (CABG). The authors aim to identify the potential risk factors that lead to SVGA in post-CABG patients.

Methods: A systematic review of original studies, observational studies, systematic reviews, meta-analyses, case studies, and case series was conducted using PubMed, Web of Science, Scopus, EMBASE, and Google Scholar involving adult patients (> 18) with SVGA after CABG using MESH terminology in a broad search strategy. All searches were performed and analyzed according to PRISMA and duplicates were removed via Rayyan. Two independent investigators extracted and assessed the data involving demographics, and baseline data related to CABG and its manifestations.

Results: Out of 487 finalized articles, 14 of them matched the inclusion requirements and reported 12 cases of SVGAs following CABG. Atherosclerosis with intimal calcification was the most common risk factor followed by infection. Others included hyperlipidemia, pneumonia, and cardiac pathologies mostly related to the ventricles and valves.

Conclusion: Atherosclerosis associated with intimal calcification is the most common risk factor. Patient outcomes seem to improve upon early identification and regular follow-up imaging. The exclusion criteria indicated the study's limits, and future studies that address these constraints may be able to better understand the risk variables involved in the genesis of SVGA.

Keywords: coronary artery bypass graft, graft aneurysm, risk factor, saphenous vein graft

Introduction

In patients with stable ischemic heart disease and significant left main coronary artery stenosis, coronary artery bypass grafting (CABG) is recommended to improve survival[1]. Saphenous vein grafts (SVG) are frequently used due to their convenient length, diameter, and wall characteristics. SVG aneurysm (SVGA) causes a rare and potentially fatal complication of CABG. SVGA occurs as a rare complication in less than 0.07% of patients following this procedure[2–5].

HIGHLIGHTS

- Saphenous vein graft aneurysm post coronary artery bypass grafting has 15.7% mortality rate prompting the identification of its risk factors.
- Atherosclerosis with intimal calcification is the most expected risk factor.
- Dyslipidemia and hypertension were the most frequent comorbidities.
- Developing a risk factor-based score system can help to choose the graft vessel type.

The first case of an SVGA was reported in 1975, but it remains an uncommon complication following CABG, occurring in less than one percent of patients undergoing the procedure[2,6]. Despite its rarity, it is a life-threatening condition, with in-hospital mortality reaching as high as 15.7%[3]. It usually takes 10–20 years after the operation for an individual to develop SVGA[4]. The real incidence is likely to be estimated due to the number of undiagnosed asymptomatic cases and uninvestigated untimely deaths concerning the severe consequences of this disease[7].

SVGA can be classified into different groups, such as early versus late or true versus pseudoaneurysm. Late aneurysm formation, may occur secondary to atherosclerotic degeneration and the exposure of high arterial pressure to the thin vein vessel wall. Meanwhile, early aneurysms after surgery can develop secondarily as a result of a number of causes such as infection of the implanted graft, intrinsic weakness of the venous wall (i.e. undetected varicosities), and technical factors relating to conduit

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harvesting, preparation, and grafting[8]. Complications might also be attributed to various factors: technical aspects such as anastomotic suture disruption, conduit injury, or the inability to reverse the SVG during grafting; atherosclerotic degeneration, infection of the implanted graft and intrinsic weakness of the venous wall[9–14].

SVGAs can clinically present in a variety of ways such as chest pain, dyspnea, syncope, hemoptysis, chronic cough, sternal/skin erosions, pulsatile mass, chronic/acute heart failure, dyspnea, and myocardial infarction[7]. The clinical presentation of SVGAs described can vary from an asymptomatic patient with an incidental radiological finding to a profoundly shocked patient with life-threatening hemorrhage secondary to SVGA rupture.

While transthoracic echocardiography may help detect mediastinal masses in individuals with cardiac symptoms suggestive of SVGA, trans-esophageal echocardiography can provide serial measurements of the size of the aneurysm[14,15]. Echocardiography, MRI, computed tomography (CT), and arteriography confirm the diagnosis of SVGA[16].

Because of the wide range of clinical presentation of SVGA following CABG and the difficulty in diagnosis despite several tools, the identification of its risk factors is crucial for prognosis and future management stratification strategies.

Methodology

Research aim

The PICO-8 model was applied based on the following criteria:
(1) P (Population): Adults (>18) with SVGA after CABG.
(2) I (Intervention): CABG.
(3) C (Comparison): Adults without SVGA after CABG.
(4) O (Outcomes): Risk factors.

Search strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) model was followed to choose the studies for the systematic review as shown in the flow diagram in Figure 1

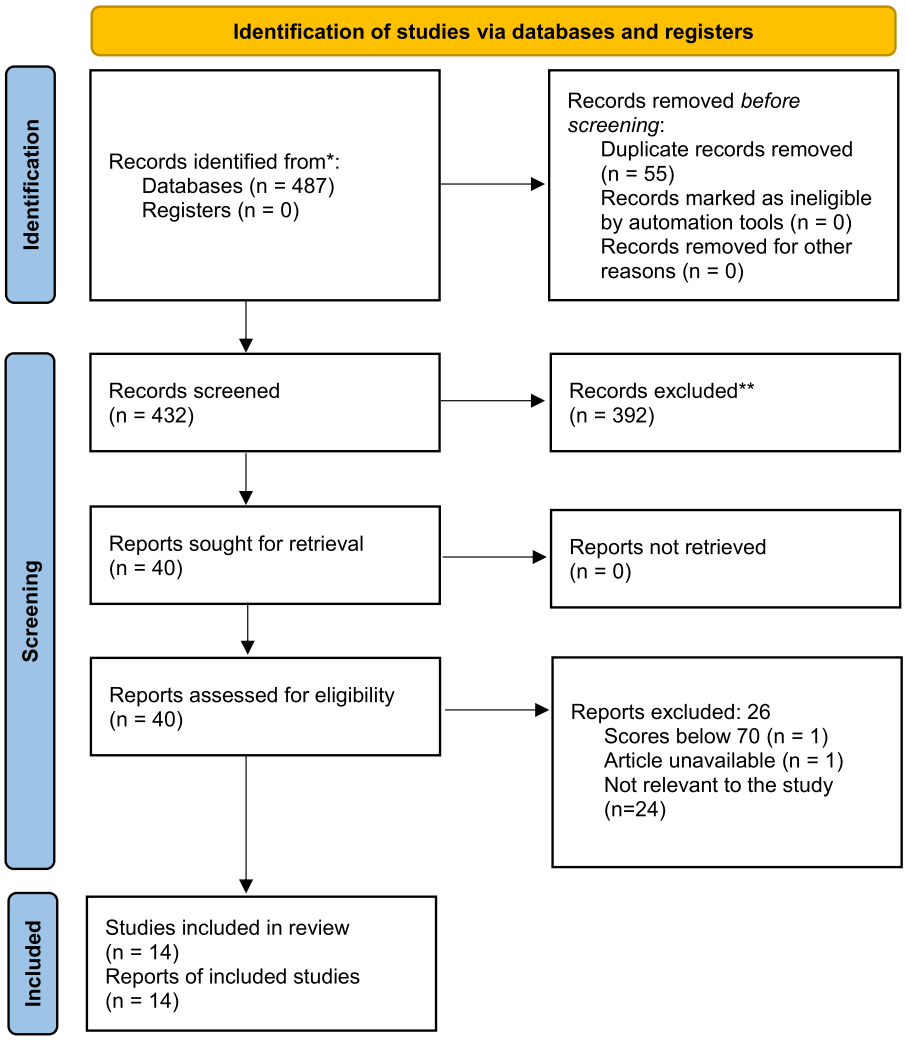

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 flow diagram for new systematic reviews which included searches of databases and registers only. *Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers). **If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools. From Page *et al*.[17].

Table 1

Detailed search strategy for databases

Database	Equation	Records identified (*n*)	Filters
PubMed	((('risk factors'[MeSH Terms] OR ('risk' [All Fields] AND 'factors' [All Fields]) OR 'risk factors' [All Fields]) AND 'aneurysm' [MeSH Terms]) AND ('saphenous vein' [MeSH Terms] OR ('saphenous' [All Fields] AND 'vein' [All Fields]) OR 'saphenous vein' [All Fields])) AND ('coronary artery bypass' [MeSH Terms] OR ('coronary' [All Fields] AND 'artery' [All Fields] AND 'bypass' [All Fields]) OR 'coronary artery bypass' [All Fields] OR ('coronary' [All Fields] AND 'bypass' [All Fields] AND 'surgery' [All Fields]) OR 'coronary bypass surgery' [All Fields])	119	Open access
Scopus	(ALL (aneurysm) AND ALL (saphenous AND vein AND graft) AND TITLE-ABS-KEY (risk AND factors) AND ALL (coronary AND artery AND bypass AND graft))	163	Open access
Web of science	risk factors (All Fields) AND aneurysm (All Fields) AND saphenous vein graft (All Fields)	30	–
Google Scholar	Coronary bypass surgery risk OR factors 'saphenous vein aneurysm'	44	–
EMBASE	('risk factors'/exp OR 'risk factors' OR (('risk'/exp OR risk) AND factors) OR 'spahenous vein' OR (spahenous AND ('vein'/exp OR vein))) AND ('aneurysm'/exp OR aneurysm) AND ('coronary artery bypass surgery'/exp OR 'coronary artery bypass surgery')	131	–

and was registered on PROPERO. Five databases PubMed/Medline, Web of Science (WOS), SCOPUS, EMBASE, and Google Scholar were searched through establishing search equations that included MESH terms (Table 1). Studies retrieved from these databases were exported to Rayyan and a search for duplicates were performed. After meticulous evaluation, all found duplicates in Rayyan were resolved.

Selection criteria

Selection criteria were based on inclusion and exclusion criteria, which were discussed among the authors and were established to include standard studies for data extraction (Table 2). Inclusion criteria include age greater than 18, original studies, observational studies, systematic review, and meta-analysis, case reports, and case series. Narrative reviews, editorials, short communications, and animal studies were excluded. Moreover, articles not published in English and articles with unavailable full text were excluded as well.

Data extraction and management

Data were extracted from each study and assessed by two independent investigators using predefined Google Sheets forms. The collected information included basic details such as the author's name, year of publication, study type, DOI, and key demographic information like age, sex, and ethnicity. Additionally, baseline characteristics such as presenting symptoms, comorbidities, CABG duration, and type of aneurysm were noted. Details about the type of intervention used and the outcomes were also gathered. Any discrepancy was resolved with the intervention of a third reviewer.

Table 2

Inclusion and exclusion criteria for study selection

	Inclusion	Exclusion
Population	Adults (> 18) with saphenous vein graft aneurysm after CABG	A. Animal studies B. Studies not published in English C. Not relevant to study D. Full text not available E. Low screening score F. Nonblinding study
Intervention	Coronary artery bypass graft (CABG)	
Comparators	Adults without saphenous vein graft aneurysm after CABG	
Study designs	Original studies, observational studies, systematic review, and meta-analysis, case studies, case series	Narrative reviews, editorials, short communications

Analysis and synthesis of data

The findings of the included studies were integrated and presented in a cohesive and narrative manner. The collected information was divided into three groups with respect to the origin of SVGA-true aneurysm, pseudoaneurysm, and congenital aneurysm. The studies were also classified according to the time of presentation-early versus late. Through this review, we were able to identify the most common presenting symptoms, risk factors, imaging modality, and line of treatment used.

Quality assessment

For case reports and case series the CARE guidelines (for CAse REports) tool was used. Other observational studies, such as case–control studies, cohorts, or cross-sectional studies were assessed using Strengthening the Reporting of Observational Studies for Epidemiology (STROBE) guidelines. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist was used to qualify systematic review and meta-analyses while JADAD guidelines were used for randomized controlled trials. Finally, ethical and bias criteria were assessed throughout the studies, which provided relevant information to answer the research question.

Evaluation of the studies

After the abstract screening, each paper was analyzed in its entirety using an Excel spreadsheet in which the study's basic data (title, type of article, author, year of publication, database used and link for full text) as well as the guideline checklist item used with the final calculated score allocation were recorded. Studies with a score greater than 70% were included in the study.

Results

An electronic search of PubMed, Scopus, Web of Science, Google Scholar, and EMBASE was performed for any literature in English and subjects over 18 years old with a history of SVG. The MESH terms included risk factors, SVGA, and coronary artery bypass. References were also reviewed for any additional cases. This search revealed a total of 487 articles. All articles were retrieved and reviewed.

Application of exclusion and inclusion criteria revealed 14 articles with 12 case reports. All articles were retrieved and studied. In our review, we included the patient's demographics, age, condition, sex, signs, symptoms, comorbidities, aneurysm type and size, the timeframe from undergoing CABG to detection of SVGA, intervention done, diagnostic modality, aneurysm type, aneurysm size, outcome, risk factors, and complications (Table 3).

The median age of the cohort was 47 years (range, 36–80 years) with male predominance and a male-to-female ratio of 5:2. The median time from CABG to a diagnosis of SVGA was 170 months (range of 10 days 336 months). We had three patients who were white and the others' ethnicity was not mentioned. The most common type of aneurysm was the true type ($n=7$, 58.3%), followed by pseudoaneurysm ($n=4$) and congenital ($n=1$). The most typical presentations were dyspnea ($n=4$), chest pain ($n=4$), and angina ($n=3$). Furthermore, only a few patients were asymptomatic ($n=3$) upon arrival. Most of the patients had hyperlipidemia ($n=7$) and hypertension ($n=6$), and diabetes mellitus ($n=2$) as comorbidities.

The most commonly used diagnostic tool was CT with or without an angiogram ($n=14$) followed by a chest radiograph ($n=12$). Adjuvant modalities were MRI, cardiac catheterization, and echocardiography.

The surgical management of choice was mainly a median sternotomy, and two cases underwent redo CABG. One case had a Dacron graft patch angioplasty. Some patients had pneumonia ($n=2$), and hyperlipidemia ($n=1$), and one patient had a wide spectrum of risk factors involving hypertrophy of both ventricles, stenosis plus insufficiency of the semilunar valves, and mitral regurgitation. Atherosclerosis ($n=7$) was the most common risk factor followed by severe intimal calcification ($n=5$).

Most patients had no complications except for thrombus formation ($n=2$), a person with pulmonary and renal insufficiency, one with blood in the upper and lower lobes, a hematoma, and another with accelerated hypertension during surgery. The most common outcome was a stable patient ($n=13$) while in one case death due to sepsis and multiorgan failure.

Discussion

One chronic CABG complication is SVGA[21]. These aneurysms are a rare complication observed in less than 0.07% of patients undergoing the procedure[5]. SVGAs to coronary arteries were first reported in 1975, yet they remain an unusual complication after CABG surgery. Wight *et al.*[20] described the differences in causes affecting the formation of true aneurysm and pseudoaneurysm.

While pseudoaneurysms are mainly because of faulty surgical techniques such as high-tension suturing or erroneous graft placement, true SVGAs are associated with atherosclerosis and hyperlipidemia[11,20,22]. In our review, most of the aneurysms identified were true, and these aneurysms developed as early as 10 days after CABG surgery and as late as 21 years. Krishnasamy *et al.*[23] described that some common initial manifestations of SVGAs are worsening dyspnea, chest pain on exertion, or dizziness. During our review, we noted that nine patients presented with clinical features suggestive of ischemia to the myocardium, hence the same clinical manifestations. Imaging studies like CXR, CT, MRI, transthoracic echocardiography, and coronary angiography were used to confirm the diagnosis of SVGA.

Several factors may contribute to the development of SVGA, such as technical issues, infections, atherosclerosis, or venous wall problems[2,10,14]. Our review found that atherosclerosis with associated intimal calcification was the most expected risk factor, followed by infection. There are some suspected causes mentioned in Abbasi *et al.*, such as necrosis and inflammation of the venous wall, atherosclerotic degeneration of veins after 8–10 years of surgery, aneurysms at the branched sites, and formation of smooth muscle in a longitudinal rather than circular fashion leading to the vicinity of venous valves. Moreover, trauma to vessels during a surgical procedure can also lead to an aneurysm in the first few months after surgery[18].

The common comorbidities were dyslipidemia and hypertension, but aneurysms were also identified in a few cases with no comorbidities. Other common risk factors included mild RVH, mild LVH, mitral regurgitation, aortic valve insufficiency, pulmonary valve stenosis, CHF, pneumonia, chronic inflammation, hyperlipidemia, intimal proliferation, and calcification. Six of the cases in our review had hyperlipidemia as a comorbidity during the diagnosis. In addition, a minimum of 10 years had passed since the CABG before an SVGA was diagnosed. These findings cement the theory that hyperlipidemia, atherosclerosis of SVGA, and a long postprocedural interval are associated with the formation of SVGA[11,19,20,22].

Surgery, percutaneous procedures, and conservative management are the most common treatment options. Surgical treatment involves ligation or resection of the graft and replacement of the conduit with revascularization of the native coronary arteries, which is the first-line management option for treating SVGA[4]. The outcomes of these options differ with mortality rates of 13.9, 6.1, and 23.8%, respectively, for surgical, percutaneous, and conservative treatment[12]. In our review, we noticed that eight patients were treated with resection of the aneurysm, with one case each of percutaneous intervention and conservative therapy. Most patients appeared stable after their surgical intervention and were discharged with improvement; the same outcome was noticed for those that had undergone percutaneous intervention and conservative treatment.

Future research could focus on developing and validating a scoring system for identifying patients at high risk for aneurysm development or progression. This system could incorporate a variety of risk factors, including genetics, lifestyle factors, medical history, and imaging findings. Additionally, studies could investigate the effectiveness of alternative vessel options in patients at high risk for aneurysm development or progression. Long-term follow-up studies could provide valuable insights into the long-term outcomes of these patients and inform clinical decision-making in this patient population. Finally, investigations into the underlying mechanisms of aneurysm development and progression could lead to the development of novel preventive and therapeutic strategies.

Table 3

Results

Study	Age	Comorbidities	Ethnicity	Key symptoms	CABG duration	Type of aneurysm	Specific intervention	Imaging	Size of aneurysm	Expected outcome	Risk factors	Complications
Abbasi *et al.*[18]	68 M	Nil	Nil	Chest pain, dyspnea, hemoptysis	1 year	Pseudoaneurysm	Surgery- median sternotomy	TTE, fiberoptic bronchoscopy, CTA	6.36 × 6.06 cm	Stable patient	mild RVH, mild LVH, mitral regurgitation, aortic valve insufficiency, pulmonary valve stenosis	Blood in upper and lower lung lobes, hematoma, thrombus
Almanaseer *et al.*[3]	75 M	Nil	Nil	Confusion, weakness	14 years, AAA repair 3 years	Pseudoaneurysm	Surgery	CXR, CT, CAG (Graft patency)	9 × 8 × 6 cm	Stable patient		
Baldwin *et al.* 1992	55 M	Heart transplant patient, Previous MI	Nil	Dyspnea	15 years	True aneurysm	Surgery-mediastinal exploration, dacron graft patch angioplasty	CXR, CT, MRI, cardiac catheterization	NA	Sepsis, MOF	CHF, graft atherosclerosis	Pulmonary, renal Insufficiency
Barnard *et al.* 2011	73 F	Smoker, hypertension, high cholesterol, + ve family history	Nil	Angina, Dyspnea	21 years	Giant calcified aneurysm	Redo coronary surgery cardio-pulmonary bypass	CAG, 64 slice CT,	NA	Stable patient	Calcified aneurysm	Nil
Chalasani *et al.* 1997	Patient 1- 77 F Patient 2- 61 F	1-Nil 2- Hypertension, hyperlipidemia	Nil	P1: admitted for Pneumonia P2: admitted for hip surgery	P1: No CABG, P2: 8 years	P1: Congenital aneurysm RCA	Surgery	Px-1: CXR, CT, MRI, Cardiac catheterization, Coronary aortogram Px-2: CXR, CT (diagnostic aspiration), MRI, cardiac catheterization	P1: 12 × 14 cm P2: 6.2 × 3.4 cm	Both patients were stable	P1: pneumonia, P2: chronic inflammation calcified intima, thrombus	P1: thrombus present P2: accelerated hypertension during surgery,
Fukui *et al.* 1998	80 F	Nil	Nil	Severe anterior chest pain refractory to nitroglycerin	10 y	True aneurysm	Redo CABG	CXR, CAG	Not mentioned	Stable patient	Atherosclerosis	
Hughes *et al.* 1991	54 M	Asymptomatic peptic ulcer disease, nephrolithiasis, type IV hypercholesterolemia, mild hypertension	White	Asymptomatic	14 years	True aneurysm	Conservative treatment	CXR, contrast CT, cine MRI, selective angiography	6 × 5 × 4 cm	Stable patient		
Pulling *et al.* 2008	61 M	Hypertension, hyperlipidemia	Nil	Episodic nonspecific chest discomfort and tightness	10 years	True aneurysm		CXR, CTA	3.9 cm	Stable patient	Atherosclerosis	
Reyhanoğlu *et al.* 2020	68			Chest pain , dizziness and syncope	10 years		Surgery	CXR, Chest CT, angiography	28 × 30 mm	Stable patient	Atherosclerosis	
Sahouri *et al.* 1995	64 M	COPD		acute dyspnea and diaphoresis	14 years	True aneurysm	Surgery	CXR, echo, cardiac catheterization, CT	5 × 7 cm	Stable patient	Pneumonia, atherosclerosis and calcification	
	70 M	Nil		Acute coronary syndrome	18 years	True aneurysm	Surgery		5.21 × 6.38 cm			

Takayama et al. 2016								CXR, coronary CTA, cardiac catheterization, echo		Stable patient	Cause otherwise not mentioned
Teja et al.[19]	36 M	Hypertension, hypercholestrolemia, diabetes mellitus, family history of coronary artery disease	White	episodic Angina	14 years	Not mentioned	Patient died of other condition, SVG aneurysm is autopsy finding		Multiple aneurysms measuring from 1–2 cm in greatest diameter	Autopsy	Hyperlipidemia, atherosclerosis, severe calcification, aortic aneurysm
Wight Jr et al.[20]	63 M	Hypercholestrolemia	White	Asymptomatic	15 years	True aneurysm	Surgery (aneurysm removed)	CXR, contrast CT of the chest, echo, cardiac catheterization	10 × 10 × 6 cm	Stable patient	Intimal proliferation and atherosclerotic plaque, focal calcification and thrombus
Yamaguchi et al. 2017	73 M	Hypertension, diabetes mellitus, dyslipidemia		Asymptomatic at arrival, SVGA detected on postoperative CAG done to check graft patency	10 days	Pseudoaneurysm suspected	Percutaneous drug eluting agent stent placed	CT, coronary catheterization, IVUS, chromaFlow imaging, optical coherence chromagraphy	Postoperative day 10 and day 18- 13 mm and 20 mm, respectively	Stable patient	No specific risk factor Nil mentioned

P1 - Patient 1, P2- Patient 2.
CAG, coronary angiography; CT, computed tomography; CXR, chest X-ray; Echo, echocardiography; IVUS, intravascular ultrasound; TTE, transthoracic echocardiography.

Limitations

The present study also had certain limitations. Firstly, the study is based on a small sample size of only 14 articles, including 12 case reports, which may limit the generalizability of the findings to the broader population. Secondly, a meta-analysis could not be conducted on the exposed variables. Thirdly, the studies available only reports a limited set of risk factors, including hyperlipidemia, hypertension, and diabetes mellitus, and may not have accounted for other potential risk factors such as smoking, family history, or genetic factors. Additionally, this systematic review may suffer from the risk of bias, clinical and statistical heterogenicity of the included studies and publication bias that might influence the study result. Future studies that address these limitations could provide a more comprehensive understanding of the risk factors of SVGA after CABG. It is worth noting that despite the limitations, the present study still provides valuable information for the medical community.

Conclusion

In conclusion, SVGAs are a rare but life-threatening complication that can occur after CABG in less than one percent of patients. This review found that atherosclerosis with associated intimal calcification was the most expected risk factor, followed by infection responsible for causing SVGA after CABG. Other common risk factors include mild RVH, mild LVH, mitral regurgitation, aortic valve insufficiency, pulmonary valve stenosis, CHF, pneumonia, chronic inflammation, hyperlipidemia, intimal proliferation, and calcification. The most commonly associated comorbidities were dyslipidemia and hypertension, but aneurysms were also identified in a few cases with no comorbidities. The future prospect of this research is to develop a score-based system on the basis of identified risk factors which will help surgeons in their decision-making regarding the choice of vessel used for graft other than the saphenous vein for CABG.

Ethical approval

Ethics approval was not required for this systematic review.

Consent

Informed consent was not required for this systematic review.

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Author contribution

B.G.: conceptualization, data curation, formal analysis, methodology, original draft, review, and editing, supervision and validation, project administration, visualization; T.S.K.: conceptualization, data curation, methodology, original draft, review and editing; J.C.D.C.M.: original draft; A.B.: original draft, review and editing; M.S.: original draft; R.B.: original draft, review and editing; F.J.V.-L.: original draft; S.M.G.: original draft; Y.A.A.: original draft.

Conflicts of interest disclosure

The authors declare that they have no financial conflict of interest with regard to the content of this report.

Research registration unique identifying number (UIN)

1. Name of the registry: PROSPERO.
2. Unique identifying number or registration ID: CRD42023 420575.
3. 3.Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=420575.

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Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

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