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***Corresponding author**
Zhiyong Liu
E-mail
2846266997@qq.com
Phone
+86 137-7062 8850

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Recent Advances in Comprehending the Incidence and Etiology of the Post-Surgical Stroke After Coronary Artery Bypass Grafting: A Systematic Review

Hussain Amjad, Zhiyong Liu*, Bukhari Ashfiq, Wei He, Xin Xue, Lei Wang, Limbu Dipsundar, Zhenye Pu

Department of Cardiothoracic Surgery, Southeast University Affiliated Zhongda Hospital, Nanjing, China

Abstract

Coronary artery bypass graft (CABG) surgery has been adopted as an efficacious treatment for patients with coronary artery disease. To date, no comprehensive report has been published on the recent advances in terms of etiology and risk factors of stroke after CABG surgery. The current review has for the first time analyzed the most recent advancements and investigations done on post-surgical stroke following CABG surgery in addition to the comprehension of the incidence of post-surgical stroke and related it to the Chinese population. Furthermore, the review has also determined the etiological parameters and risk factors leading to post-surgical stroke. This comprehensive review suggests the incidence of post-surgical stroke within a few days of the surgery and varies considerably due to different mechanisms blocking the supply of blood to the brain and hampering the normal functioning. The Chinese population has seen an alleviation in the post-surgical stroke after CABG for the last decade due to technological advancements; however, the lack of knowledge regarding risk factors still needs to be addressed meticulously by cardiac surgeons in China and other regions of the world. Furthermore, different risk factors, *e.g.*, an age >70 years, female sex, hypertension, kidney failure, diabetes mellitus, smoking, peripheral artery disease, 40% ejection fraction, previous history of any type of stroke, and calcification of aorta, etc. have been known for augmenting the chances of post-surgical stroke incidence.

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Introduction

Contemporary decades have been marked by astonishing advancement in the arena of cardiac jarrahs. Despite such progression, the occurrence of neurological impairments following cardiac surgery is inevitable. Among such neurological complications, post-surgical stroke has been identified as one of the most annihilating impairments following coronary artery bypass grafting (CABG). Different cardiovascular methods have been devised for the significant alleviation in stroke, *e.g.*, CABG, isolated valve surgery (IVS), and carotid endarterectomy (CEA) [1]. Being a major factor for devastating the patient's health and physical integrity and functionality, stroke following CABG surgery has also been known for severe economic reverberations. With an ever-augmenting statistics, stroke has been known for impacting more than 21,000 patients in the United States of America in addition to 42,000 patients on a global scale. Such a debilitating patient statistic is subsequently associated with the incurrence of health care costs, raising up to 2 – 4 billion dollars every year. Special investigations have been carried out to comprehend the underlying mechanism and responsible risk factors leading to stroke as a post-surgical impact of the CABG surgery and resulting in an amplified mortality rate. In this regard, a myriad of the mechanisms with respect to patients' physiological being and procedural steps have been identified that plays an influential role in the intensification of the plausibility of the stroke after CABG [2, [3].

The association of the stroke with CABG as a post-surgical complication has been justified by the fact that its occurrence is exactly in the primordial stage of the CABG surgery and thus, accounting for the substantiation of the fact that there is a direct proportionality between the stroke incidence and the operational procedures [4]. CABG surgery has been used in a widespread manner around the globe for many decades; however, there is considerable controversy about the pros and cons of CABG surgery. Generally, cardiac surgeons prefer off-pump CABG for the prevention of negative implications associated with the cardiopulmonary bypass (CPB) which leads to the dysfunctionality of the patients' multiple organ systems by activating the mediators having coagulative and inflammatory action [5]. However, the preference of the off-pump CABG over CPB is yet associated with serious complications, *e.g.*, hepatic, respiratory, kidney and multi-organ failure, coagulative impairments, neurological complications and myocardial infarctions in addition to stroke. Such complications are more pronounced in patients having the previous history of the antecedent comorbidities [6]. Nevertheless, the rigorous researches on risk factors and advancement in the technological facets have caused an alleviation in the occurrence of stroke in terms of both surgical steps and percutaneous intercessions [7, 8]. The innovative technological transformations in cardiac surgery, *e.g.*, carotid artery stenting (CAS), minimally invasive (robotic) mitral valve repair surgery, and transcatheter aortic valve replacement (TAVR), etc. have also been primarily examined for their potential in reducing stroke in comparison to the pre-existent surgical counterparts. Stroke accounts for 1% and 5% of the isolated CABG surgeries carried out around the globe [9, 10]. Though different studies have focussed on the comprehension of the stroke in an absolute manner in the patient population undergoing surgery; nevertheless, the more effective mode of reducing stroke incidence is based on the clear understanding of the background risks so that the communication between the patient and the surgeon is effective enough for better decision making prior to surgical operation [11-13].

The calculation of the relative risk of stroke incidence following CABG surgery and later comparing it with different surgical populations is not an effective practice. The long-term consequences of stroke following CABG have been investigated in various clinical series. In this regard, the results of different studies are supportive of the suitability of percutaneous coronary intervention (PCI) over CABG surgery for giving rise to an alleviated 5-year stroke. This fact is true for patients having multi-vessel and left main coronary artery disease (CAD). Both PCI and CABG possess similarity for leading to stroke incidence between 31 days and 5 years, particularly the stroke incidence has been more pronounced after CABG in patients having an earlier history of multi-vessel disease and diabetes mellitus. The higher risk of death in patients within 5 years, having post-surgical stroke has been reported within 30 days of revascularization in comparison to patients without stroke [14]. The favourability of CABG surgery in terms of effectiveness has been embraced around the globe. In addition to the most cherished aspects associated with the CABG procedure, there are also some considerations, cardiac surgeons must focus

on the enhancement of the patient health quality in the long term. In achieving this goal, one of the challenging tasks is the correct identification and intervention of the associated risk factors giving rise to different complications following the CABG surgery. Post-surgical stroke has been one of the major and highly prevalent consequences of CABG; however, to date, no comprehensive work has been published outlining the recent advances, characterization, prevalence and etiological aspects of the post-surgical stroke. Therefore, the current review has been done to clearly elucidate the recent advances and the status of the post-surgical stroke following CABG around the globe. Furthermore, the authors have attempted to include a Chinese perspective in this arena due to the larger proportion of the CAD patients residing in China and are being treated with CABG.

Data Collection

The investigation of recent advances in the post-surgical stroke following a stroke, identification, risk factors and addition of Chinese context was done by the thorough searching of Medline, PubMed, Cochrane, Google Scholar, NHS Evidence and Web of Science databases until March, 1st 2019. Researches, case studies and statistic reports were meticulously comprehended and the searching standard on the aforementioned databases were varied as ["Stroke as post-surgical impact of CABG" OR "Risk factor for stroke following CABG" OR "Etiologic parameters of stroke after CABG" OR "CABG and stroke in Chinese perspective"] either in the title or abstract. Articles published in the English language were preferred over other languages. The review was inclusive of the literature review from 2000 – 2019 but no boundaries were set and articles before 2000 were also studied scrupulously. The description of the data in the current review has been limited to 200 articles considering the relevancy of topic, space and peer review convenience. Special care has been taken in the omission of the facsimile versions and false positives. Furthermore, the figures adopted from other researchers have been used after permission from the publishers and due share was given by citation of the author and publisher having the copyright of the material.

Results Analysis

Characterization of stroke

In the historical perspective, there has been an existence of significant multifariousness in characterizing stroke in terms of definition. Therefore, surgeons have been facing difficulty in the comparison of previously existing surgical research publications and recently occurring clinical trials operated with different procedures. Newly occurring neurological disorder within a month after CABG surgery is known as a perioperative stroke (Fig. 1). While, stroke is often referred as a neurologic disorder impairing the functionality of the motor, sensory, or cognitive entities having a persistent pattern of more than 1 day, often leading to death and is not explained in terms of other neurologic events, *e.g*., postoperative delirium, dementia, and head trauma. The perioperative stroke risk is considerably lower in case of other surgeries, but CABG and neurosurgeries are often known for giving rise to ischemic stroke up to 3 months [15]. Perioperative stroke accounts for one of the most annihilating impacts occurring after CABG and contributes influentially in augmenting morbidity and mortality with a 5-fold increment. Furthermore, it also incurs heavier capital costs of health care resources. The incidence of postoperative stroke spans over a range of 0.8 - 5.2% of the patient population having undergone CABG surgery [16].

There has been considerable evidence regarding the majority of strokes occurring postoperatively, while a diminutive fraction occurs

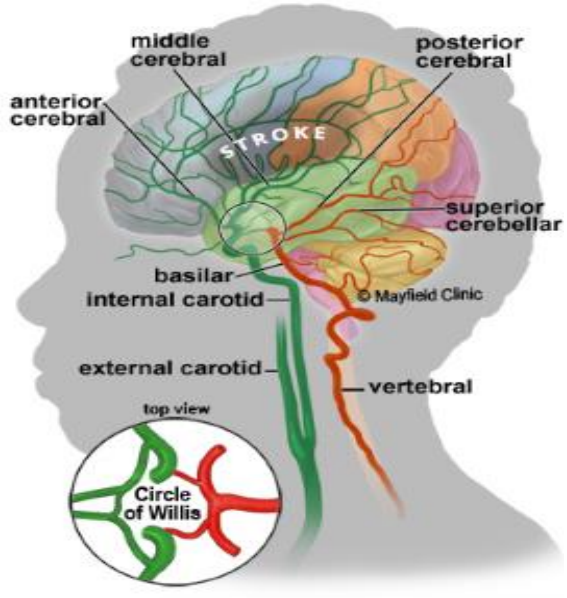

Fig. 1 Stroke explained diagrammatically. Stroke refers to the sudden discontinuation of the blood supply to the brain. Stroke often causes the occlusion of the middle cerebral artery. Reproduced with permission from Ringer and Jimenez [23] Copyright of Mayfield Clinic, Ohio (2018).

Table 1 Risk of post-surgical stroke following CABG surgery reported from different parts of the globe.

Study	Study duration	Type of surgery	Type of stroke	Region	Comments
Higgins et al. [28] (n= 10,085)	April 2007 and Dec. 2012	Primary isolated CABG, valve, or combined CABG/valve surgery	Peri-operative	Canada	The risk of 5-year mortality has resulted from stroke following CABG surgery.
Moss et al. [29] (n=12,079)	2002 to 2013	Primary, isolated CABG	Post-operative	US	Post-surgical stroke is enhanced by clamping of the aorta during CABG surgery.
Nasreen et al. [30] (n= 80)	1st Feb. 2014 to 31st Jan. 2015	Conventional CABG	Post-operative	Pakistan	Post-operative stroke often results from extended cardiopulmonary bypass timings.
Schulman et al. [31] (n= 2264)	Jan. 1, 2000 to Dec. 31, 2003	Isolated CABG	New atrial fibrillation and resulting stroke	Canada	There is a limitation associated with the warfarin utilization for prevention of stroke after CABG.
Djokic et al. [32] (n= 680)	NS	Conventional CABG	Ischemic stroke	Serbia	Ischemic stroke is frequent result after CABG surgery in patients characterized with hypertension
Cheng et al. [33] (n= 2761)	1999 – 2011	Staged CABG and CEA	Perioperative stroke	US	Different risk factors contribute to the incidence of perioperative stroke following CABG
Chen et al. [34] (n= 1010)	2001 - 2012	Off-pump coronary artery bypass	Early and delayed strokes	Taiwan	The risk of post-surgical stroke can be considerably reduced by systematic OPCAB
Stein et al. [35] (n= 14, 000, 000)	Year 2013	Multiple cardiac procedures	Perioperative stroke	US	Patients having undergone CABG and other cardiac procedures present an augmented rate of readmission to the hospital due to the incidence of ischemic and hemorrhagic stroke.
Kinnunen et al. [36] (n= 1,314)	June 2006 to Dec. 2013	Off-pump CABG	Atherosclerotic stroke	Finland	Atherosclerosis of the ascending aorta act as an independent factor of post-surgical stroke
LaPar et al. [37] (n= 57,387)	2001 - 2011	Conventional CABG	Postoperative stroke	U.S.	Higher rates of mortality and morbidity are associated with post-surgical stroke as expressed by results from different institutions

NS= not mentioned

intraoperatively [17]. Since the CABG surgery has been frequently performed for treatment of CAD patients around the globe with 650,000 procedures per annum in the US; thus, an additional cost of $15,468 per patient is inflicted due to post-surgical stroke. Out of these 650,000 CABG procedures, 5,000 – 35,000 cases of post-surgical stroke are reported, thus signifying the influential role of CABG in giving rise to perioperative stroke [18]. There is a bimodality in the distribution of the perioperative stroke incidence timings. Firstly, there is an immediate identification of the stroke events (about 45%) right after 24 hours of surgery. While there is also a 55% incidence of different intraoperative events taking place within one hour of the CABG surgery after restoration from anesthesia. The appearance of prior embolism can be attributed to the maneuvering of the heart and aorta in addition to the particle transportation by CPB. These events are often due to atrial fibrillation, myocardial infarction (MI) and coagulative disorders. It is also an established fact that there is an enhanced chance of ischemic stroke in patients with a previous history of carotid stenosis (CS). Patients suffering from CS, when having undergone CABG, often suffer from post-surgical ischemic stroke is due to embolism, contributing up to 62% of ischemic events [19-21]. There is a scarcity of data available for comprehension of the risk profiles up to 3 months in patients having undergone CABG surgery and discharged from hospital. In the case of intracerebral hemorrhage or the blockage of the large vessels, post-surgical stroke can also result in the death of a patient. In such circumstances, the final decision for neurosurgical (NS) procedure for saving a patient's life is a challenging task [22]. The sound management strategies must be inclusive of the comprehension of the epidemiological aspect in the existing time for the development of the

predictive model so that it can be employed on the currently treated patients.

Post-surgical stroke prevalence

The incidence of stroke in different parts of the world has been pronounced and special measures have been currently employed and explored to reduce the risk of post-surgical stroke prevailing in different regions as shown in Table 1. The frequency of atherosclerosis following CABG surgery in patients has been quite pronounced but the incidence of stroke has been considerably reduced. However, the prevalence of stroke after CABG surgery is yet an alarming factor that needs to be comprehended well for the correct identification of the frequency and etiological parameters [24]. World population has a marked degree of heterogeneity and racial individualities have been undergoing CABG surgery and faced with 2.6% of post-surgical stroke incidence. Epidemiologically, stroke following CABG surgery has been accounted for 0.8-5.2% incidence [25, 26]. However, post-surgical stroke being the major cause of morbidity after CABG surgery has been reported for 1.3% incidence in the year 2017 according to the STS database, which signifies an alleviated trend in comparison to 2006 statistics. Emboli resulting in stroke due to ascending aorta is often associated with the frequent incidence. Off-pump coronary artery bypass (OP-CAB) and port-access coronary artery bypass (PA-CAB) in combination with the minimal aortic interventions and prevention of fragmentary or integral cross-clamping of aorta might subsequently lead to the extremely lower rates of stroke incidence, *i.e.*, 0.35% [27]. Since the studies published before 2010 are indicative of the patients' statistics of the 1980s or 1990s period. Therefore, the older studies do not completely refer to the currently existing trend of post-surgical stroke [38, 39], but provides a clear alleviation in the incidence due to the utilization of technologically advanced modes of operation. The incidence of post-surgical strokes in different racial groups is shown in Table 2. Patient prognosis having a stroke following CABG surgery is often based on the realistic examination of different parameters since there is a considerable degree of variation existing among the patients and clinical procedures in terms of short- and long-term consequences. Additionally, there is a clear exhibition of the specific cerebral infarction arrays in the patients developing stroke after CABG surgery. Such results act as a facilitator factor for the re-investigation of etiological aspects of stroke and are suggestive of the fact that future interventions for stroke must be based on the incorporation of the multitudinous significant mechanisms [40].

Table 2 Significant geographic disparities in the incidence of post-surgical stroke in the year 2018 [41].

Ethnic/ racial group	Stroke incidence (%)
Non-Hispanic whites	2.6
Non-Hispanic blacks	4.1
Asian/Pacific Islanders	1.5
Hispanics (of any race)	2.3
American Indian/Alaska Natives	5.2
Multiracial people	4.7

Recent post-surgical stroke cases

For the betterment of patient undergoing CABG surgery, cardiac surgeons must assure the prompt cognizance of the neurological complications. Post-surgical stroke being the most debilitating outcome of CABG surgery has been known for its lethality. Especially, the situation of the patient is challenged in worst situations, *e.g.*, the occurrence of hemorrhage or large infarction. The analysis of long-term impacts of CABG in both medical and surgical aspects expressed the susceptibility of the patients with neurological disorders despite neurosurgical interventions in the long term. Thus, the surgeons must communicate these facts of comparatively increased mortality and worst long-term consequences prior to taking neurological or cardiac procedures [42]. The failure of off-pump CABG in the assuagement of stroke rates analyzed recently in multi-center trials done in a randomized manner are indicative of the occlusion of performance of off-pump CABG by multitudinous patho-driven mechanisms and abstruseness of the surgical process [43]. Patients with suffering from recurrent atrial fibrillation (AF), a post-surgical stroke, must mandate their long term follow-ups in a meticulous manner since post-operative AF is often associated with the causing complications in both cardiac and non-cardiac surgeries [44]. The development of diverse neurological complications following CABG is often associated with an extended duration of hospitalization and death rates even in those patients that are not confirmed with stroke through radiological evidence. The evidence for a considerable reduction in the prevalence of stroke as a post-surgical impact of CABG has been strengthened by the number of investigations.

The prevalence of lower stroke rates can be attributed to the utilization of singular clamping techniques, flooding of CO, proper regulation of the high perfusion pressures, considerable hematocrit on bypass, and hypothermic conditions. Carotid artery stenosis (CS) having bilateral internal specifications done in patients is clearly indicative of the patients' vulnerability to atherosclerosis. The meticulous analysis of pre and post-operative variables expressed the role of internal CAS in enhancing the chances for neurological complication incidence as shown in Fig. 2 [45]. A group of cardiac surgeons has also investigated the influence of asymptomatic unilateral and bilateral CS as a prognosticator of the post-surgical stroke in patients suffering from stroke hospitalized after CABG surgery with an aim to gain a clear comprehension of the patients having a higher vulnerability towards stroke and also to devise an effective managerial strategy to manage this complication. Trends of the post-surgical stroke from 1999 to 2011 were also analyzed. The results of the study were supportive of both unilateral and bilateral CS as the risk factors for post-surgical stroke after CABG surgery [46].

AF is one of the most significant risk factors that give rise to stroke following CABG. The reports on the relationship between the risk factors and incidence and severity of the acute ischemic stroke (AIS) have been scanty. Meticulous investigation of the influence of hypertension and previous history of heart failure (HF) on the severity of stroke in the CABG post-surgical phase has expressed the likelihood of AIS with an elevated severity. Furthermore, HF is also a significant self-regulating prognosticator of the functional disruption following two years of stroke [47]. For the achieving best possible results with CABG in preventing and minimizing post-surgical stroke, aortic no-touch off-pump technique (anOPCAB) can be used effectively [48]. Stroke risk profiling within three months of the CABG surgery has been evaluated by utilization of the case-crossover design for the correct examination of the risk of ischemic stroke in patients undergoing CABG surgery [49].

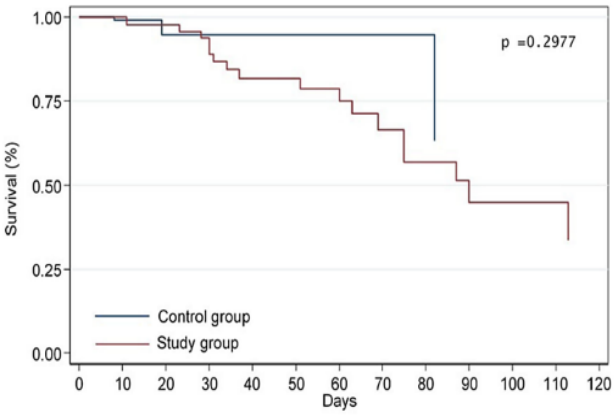

Fig. 2 Trend of mortality in the control and experimental group in the hospitalization phase represented via Kaplan Meyer Curve. Reproduced with permission from Raffa et al. [45]. Copyright of BioMed Central (2018).

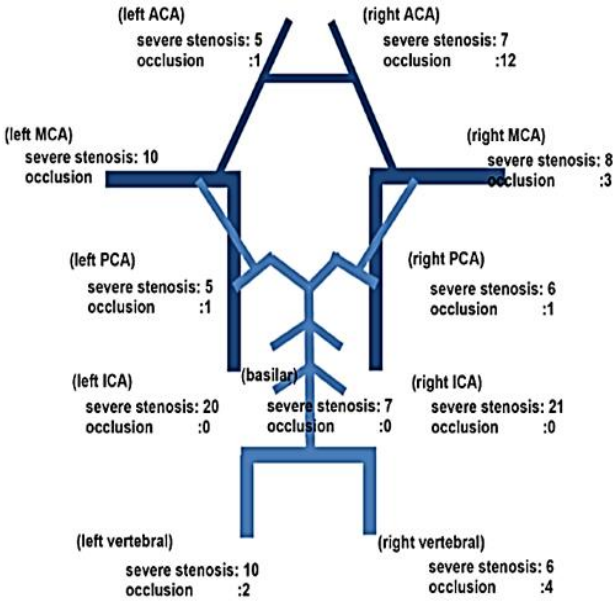

Fig. 3 Dissemination of intracranial arterial stenosis (≥70%) and obstruction magnetic resonance angiography. Reproduced with permission from Imura et al. [50]. Copyright of Scientific Research Publishing (2018).

Recent mitigative measures of stroke

Researchers have investigated the useful strategy for the prevention and management of stroke by means of controlling the most significant contributing factor, *i.e.*, the intracranial arterial steno-occlusive lesion (IAS; Fig. 3). The utilization of the magnetic resonance imaging/angiography (MRI/A) for the evaluation of IAS for the management of perioperative stroke has resulted in the positive management of stroke in patients undergoing CABG as shown in Fig. 4 [50]. Patients suffering from AF are often characterized by a left atrial appendage (LAA) for being the source of more than 90% of the analyzed thrombi. Hence, the ligation of LAA can be used as an effective strategy for the reduction of the post-surgical stroke. The existing studies based on the evaluation of the LAA ligation in the randomized control trials are non-

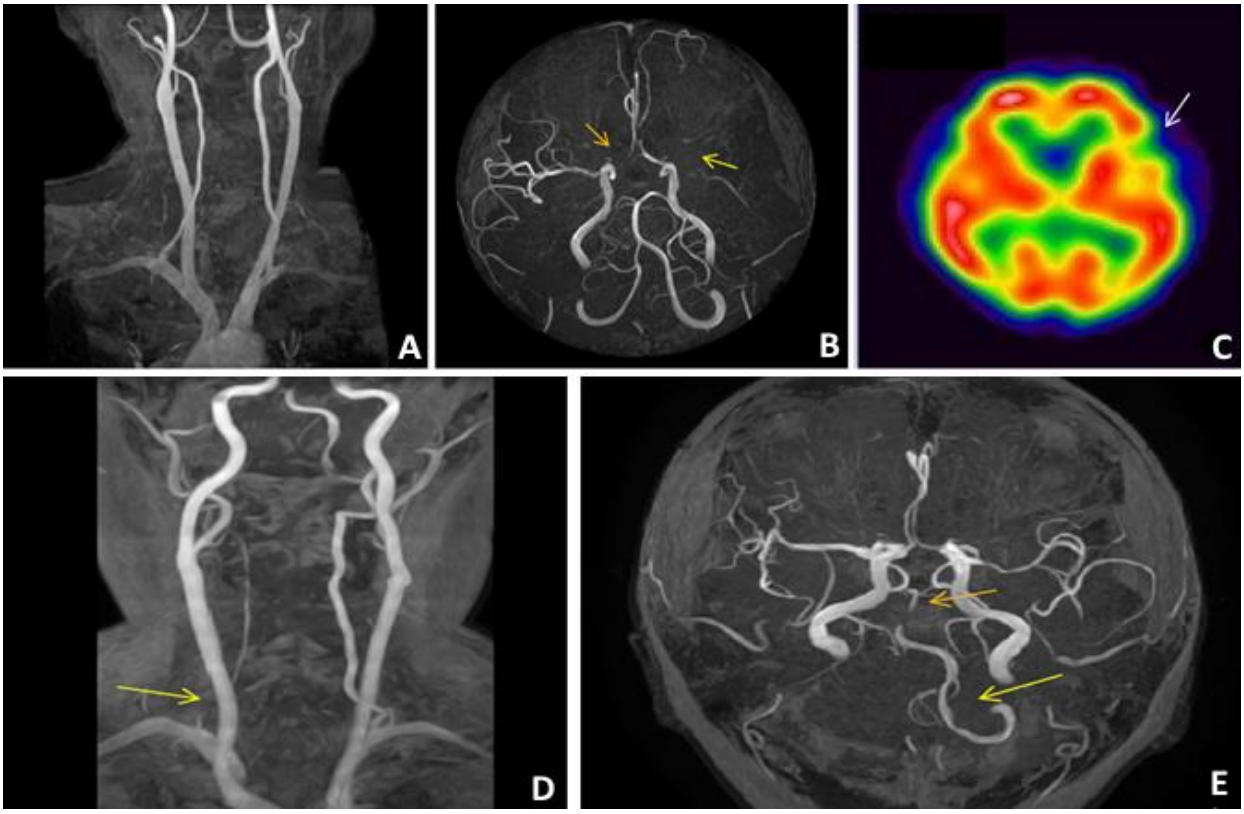

Fig. 4 Analysing the influence of the managerial strategies for post-surgical stroke incidence following CABG. No observation of noteworthy atherosclerotic lesions in MRA; (**A**) intracranial arteries with severe steno-occlusive lesions, (**B**) obstruction of a left middle cerebral artery marked by the yellow arrow, severe stenosis expressed by the orange arrow, (**C**) white arrow showing the hypoperfusion of the left middle cerebral artery. Occlusion of the right vertebral artery was found; (**D**) echo examination, and (**E**) yellow arrow showing stenosis of the left vertebral artery and an orange arrow showing basilar artery occlusion. Reproduced with permission from Imura et al. [50]. Copyright of Scientific Research Publishing (2018).

specific. Such nonspecific nature of previous investigations can be attributed to the technical challenges faced for the complete achievement of the LAA looping. Investigation in solving this challenge has recently been done by examining the role of surgical LAA ligation and the frequency of the in-hospital stroke after CABG surgery in patients characterized by the AF. Results expressed the non-association between LAA ligation and the alleviation in the post-surgical stroke [51].

The assessment of the compounded CABG and CEA operated on patients and later developing post-surgical stroke expressed the strong correlation between the compounded surgeries and the rate of the mortality and morbidity in hospitalized patients. Recently done studies have nullified the previously existing concept of CEA known for mitigating of stroke prevention by 3-5% appearing after CABG surgery. Compounded CABG + CEA have expressed a profound similarity in escalating the stroke risk with equal efficaciousness. Better preventive modes for minimization of the risk of ischemic stroke are needed for a complete assessment of the risk-stratification incorporating the compounded CABG + CEA [52]. Ischemic stroke also appears as a post-surgical impact of CABG and other Cardiothoracic surgical (CTS) operations due to large-vessel occlusion (LVO). LVO based strokes can be effectively cured with endovascular treatments. Recently done evaluations on the basis of experience with CABG patients revealed that LVO is associated with complicating the diminutive proportion of the patients following CTS and might contribute to the prolongation of aortic cross-clamping and bypass timing. There has been an achievement of positive transformation in the complication profiles of the CABG and CTS via stroke treatments done by endovascular modes [53].

Chinese nation and CABG post-surgical complications assuagement

Due to rapid urbanization, industrialization and shift from farm-based food to processed junk, the Chinese nation has witnessed a colossal enhance-

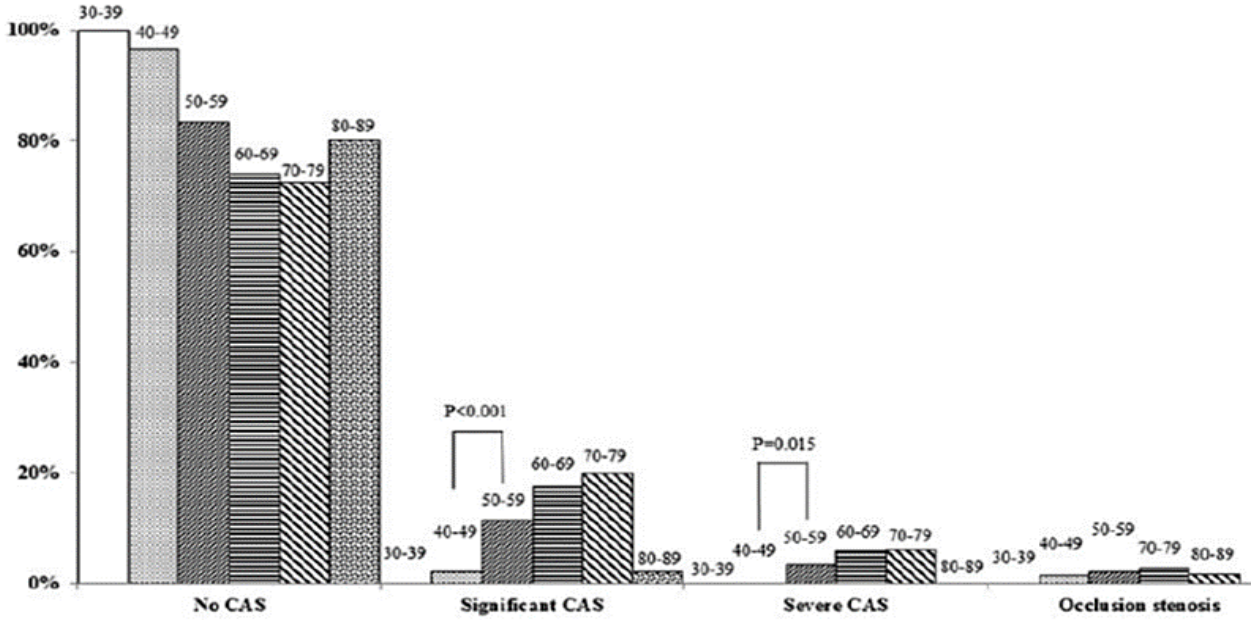

Fig. 5 Severity distribution of carotid artery stenosis (CAS) in different age groups acting as the highest risk factor for the incidence of post-surgical stroke. Reproduced with permission from Cheng et al. [62]. Copyright of Wolters Kluwer Health (2015).

-ment in the frequency of CAD since 2000 and is referred to as an epidemiological transition [54, 55]. Chinese surgeons like other parts of the world, preferring CABG is due to its safeness and effectiveness in terms of operative, anesthetic and post-surgical mitigation [56]. Despite the rapid growth of CABG surgery in China, the knowledge regarding performance at hospital level remains scanty. The characterization of the hospital's performance recorded in the national registry of China is indicative of the low-level mortality and complications following CABG surgery as per Chinese Cardiac Surgery Registry (CCSR). Furthermore, there is also a variation observed in different regions of China. Further improvements are being done for reducing CABG related complications [57]. However, the last decade has witnessed greater improvements in different urbanized teaching hospitals for truly comprehending the incidence of types and rates of complications, mortality rates and other impacts [58].

For the immediate fulfillment of the needs of the CAD patients, necessitating revascularization, different institutions, surgical specialists and young doctors in China have been designated for accomplishing CABG surgeries. Though many institutes have been technologically advancing in achieving the best possible preventive mechanisms for CABG patients, yet the geographically and population-wise gigantic territorial boundaries have been marked by contradiction in comprehending the Chinese patients risk profiles [59]. A recent investigation of a variety of hospitals of both teaching and urban sort in China and US from 2011 – 2013 have expressed the greater propensity of the Chinese nation towards CAD and thus, declared the prospects of improvement in the CABG procedures in China [60]. Coronary artery revascularization therapies (CART) like CABG and PCI have been known for improving the health of the patient in both phases of hospitalization and long-term consequences in the Chinese nation. These results are particularly obtained for patients having an acute myocardial infarction (AMI) and ischemic stroke [61]. The major complications appear after CABG surgery in different hospitals in China are not different from other regions for inflicting patients with post-surgical mortality and extended length of stays (LOS) at the hospital in addition to the other events, *e.g*., stroke, kidney failure, AMI, reoperation for bleeding [58]. Chinese CABG patients treated by a group of surgeons who have closely followed the CABG guidelines on the basis of analytical results obtained from Chinese CABG patients in a large cohort study. A set of strategies for the treatment of CAD patients in US and Europe is supportive of the fact that CAD patients having their age over a range of 65–70 years with risk factors for atherosclerosis must be carefully

screened prior to CABG surgery for the incidence of extracranial CAS, so that proper risk assessment for post-surgical stroke can be done. Chinese surgeons concluded that Chinese patients undergoing CABG and are being smokers of more than 50 years age must be exposed to pre-surgical screening for CAS for risk assessment of stroke [62] (Fig. 5). A study by Miaoa et al. [63] confirmed the role OP-CAB in reducing the prevalence of post-surgical stroke in aged patients but there is an urgent need to confirm this finding at different centers and a large number of samples. Determination of the prognosticators of CAD in Chinese patients with paroxysmal AF expresses the co-existence of the CAD and CAS. Around 32.3% of Chinese patients having paroxysmal AF suffer from CAD and the co-prevalence of CAD and CAS is calculated to be affecting 7.8% of patients [64]. The meta-analysis of 24,127 Chinese patients comprising of the 22 studies, 3 randomized control trials (RCTs) and 20 non-RCTs expressed the favourability of off-pump in comparison to on-pump CABG for reducing extended hospitalization and mortality [65]. The research groups of Chinese surgeons [66] also emphasized on the utilization of the assessment scales for stroke to enable the detailed comprehension of the stroke so that improvements can be made for the better quality of patient's health taking into account the prognostic factors.

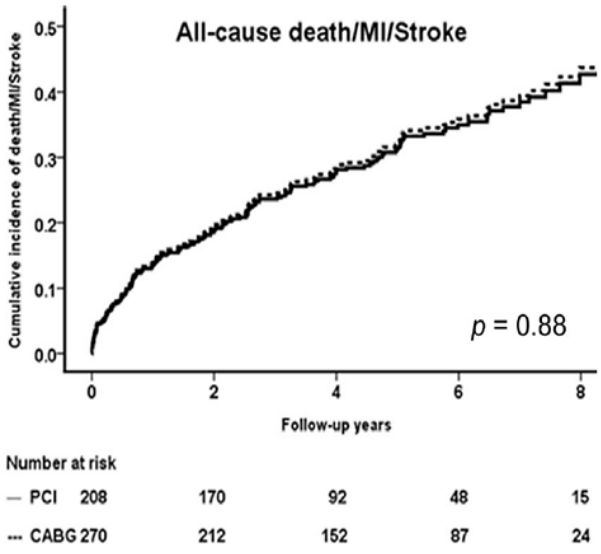

Fig. 6. The trend of cumulative incidence of all-cause death/MI/stroke. Reproduced with permission from Lu et al. [67]. Copyright of Chinese Medical Association and Elsevier Taiwan LLC, (2015).

The comparability of PCI to CABG for Chinese patients for unprotected left main (LM) CAD has expressed an ambiguity in the practical aspect. Assessment of the long term consequences of the LM CAD treated via CABG or PCI by means of stenting shows the alternativeness between CABG and PCI; however, the patients expressed a need for the repeated revascularization after PCI [67] (Fig. 6). Post-surgical complications of CABG are inevitable and risks of these complications are assessed by means of different evaluation systems (ES). The number of risk ES (RES) has been developed for perfect prediction of risks, *e.g.*, the European System for Cardiac Operative Risk Evaluation (EuroSCORE) and the Society of Thoracic Surgeons (STS) score. In China, a relatively new RES based on >9,000 Chinese CAD patients was published in 2010 and is known as Sino System for Coronary Operative Risk Evaluation (SinoSCORE). SinoSCORE has been employed in a variety of studies, including investigation of the postoperative cognitive dysfunction (POCD) in Chinese population and it expressed the increased vulnerability of the Chinese population to POCD [68]. However, despite the prognosticators and RES, there is always some information lacking regarding the characterizable risk factors giving rise to stroke following CABG surgery. Studies based on Chinese patients have pointed towards irregular angina, LVEF ≤50%, post-surgical AF, and hypotension as the risk factors giving rise to the periodic stroke [69].

Etiological parameters of post-surgical stroke

A wide range of etiological parameters has been marked for their causatives of various complications following CABG surgery, one of which is the neurological impairment known as the post-surgical stroke. Different types of strokes (Fig. 7) might prevail following CABG surgery. Generally, the embolic stroke appearing after CABG procedure is associated with the manipulation of the aorta, *e.g.*, clamping, and cannulation in addition to the sandblasting effect of flow by means of aortic cannula against the aortic wall. In addition, the comparatively larger emboli escaping the arterial pump line filter are also a major contributing factor of embolic stroke, the large emboli usually consist of air, platelet, and thrombin conglomerated mass. Furthermore, embolic stroke also results from the cardiac surgeries inclusive of the left heart carrying the risk of a bubble, particulate matter, and thrombus to the

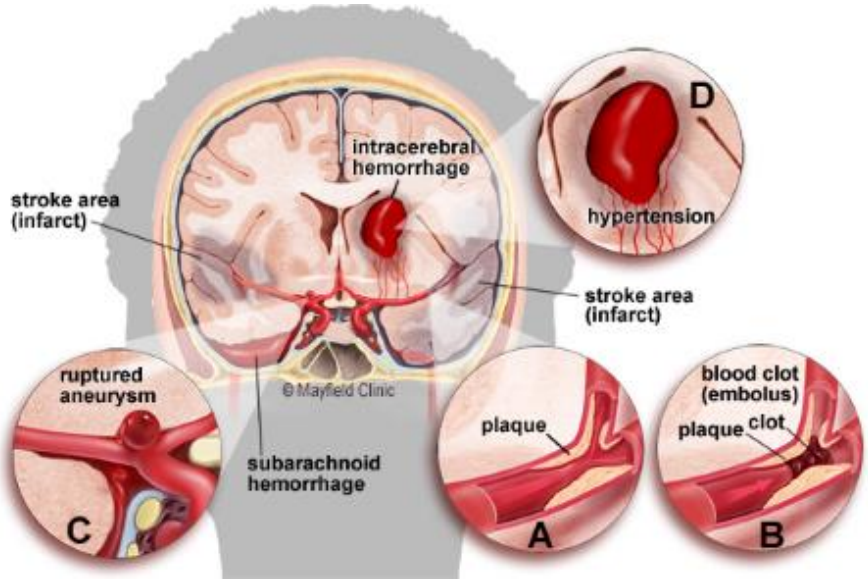

Fig. 7. Different risk factors are responsible for stroke incidence. There are a considerable variation in stroke prevalence: (**A**) atherosclerotic plaques forming ischemic stroke, (**B**) blood clots sticking to plaques and breaking off leading to embolic stroke, (**C**) bleeding in the subarachnoid space causing hemorrhagic stroke, and (**D**) tiny vessel disruption due to hypertension causing an intracerebral hemorrhage. Reproduced with permission from Ringer and Jimenez [23], Copyright of Mayfield Clinic, Ohio (2018).

brain and hence impeding its normal functionality. Embolic showers due to atheromatous debris or cholesterol may lead to watershed infarction. In the case of CABG surgery, a wide range of risk factors and underlying mechanistic reasons (Fig. 8) have been identified for causing post-surgical stroke [70, 71]. Among them, ischemic stroke has been the most preventable form as a post-surgical complication of CABG. However, apart from the established risk factors and mechanisms giving rise to stroke, there are some unconventional causes of post-surgical stroke. They can be the paradoxical embolism arising from the post-surgical deep-vein thrombosis, especially in those patients that have patent foramen ovale. Neck manipulations/hyperextension may also result in the extracranial carotid- or vertebral-artery segmentations during different surgical procedures [19].

Various origins have been identified for the occurrence of thromboembolic ischemic episodes. Possessing a close similarity with native apoplexy, thrombus can be formed in different places, *e.g.*, left atrium, ventricle, etc. Usually, the thrombi formation is a good factor during surgical operation due to an inflammatory systemic response consequently activating the coagulative system. Recent investigations showed the association of the post-surgical stroke with the location and demographical aspects, previous history of CAD, complications, hospital-based fatality and readmissions. However, there is no correlation between stroke and size of the hospital [72]. Patients undergoing CABG have also been reported to develop brain infarctions in addition to stroke when detection was done via diffuse-weighted imaging after three days of the CABG surgery [73].

Risk factors

Chronological investigations on CABG have pointed towards different risk factors, *e.g.*, advancing age, predecessor stroke and cardiac surgery, AF either pre or post-surgical, diminutive body surface area, meagrely functioning of the left ventricle, CAD and peripheral vascular disease (PVD) [74]. Furthermore, some researchers most specifically defined the risk factors as an age >70 years, female sex, hypertension, kidney failure, diabetes mellitus, smoking, COPD, peripheral artery disease (PAD), 40% ejection fraction, previous history of any type of stroke, CS, calcification of the aorta, CPB surgery, etc. [19, 75-77]. In the case of post-surgical stroke appearing after CABG surgery, there are two types of risk factors, static and transmutable. Firstly, the type of risk factors that cannot be transformed by any means like age, sex, family history, etc. While transmutable factors can be modified by means of different treatments, *e.g.*, hypertension, smoking, and hyperlipidemia. The seriousness of postsurgical

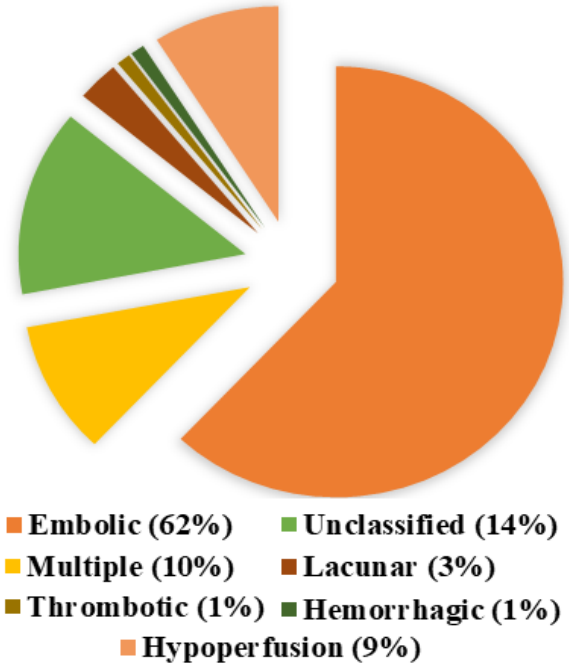

Fig. 8 Different mechanisms of perioperative stroke [70].

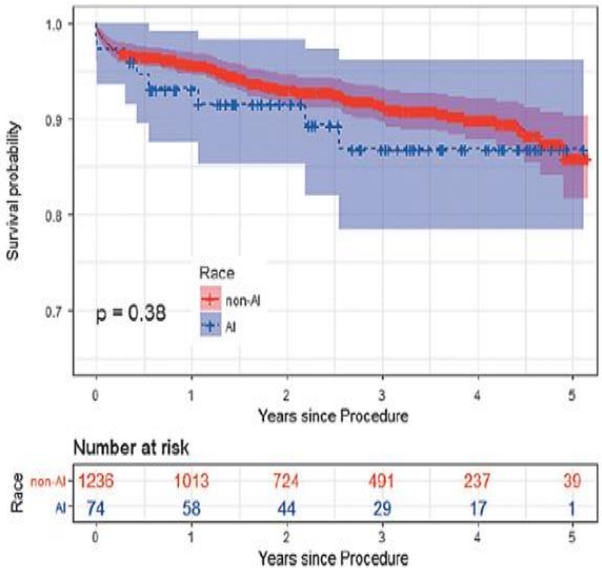

Fig. 9 Estimation of the survival rate for patients undergoing CABG surgery by utilization of the Kaplan–Meier survival estimation. Estimates for 5 years have no significant difference between American Indian and non-American Indian patients. Reproduced with permission from Anderson et al. [95], Copyright of Mary Ann Liebert, Inc. (2018).

stroke can be comprehended from the fact that there is a considerable mortality rate up to 14-21%, accounting for 10-fold augmentation in comparison with patients without developing stroke after CABG [78]. Post-surgical embolic stroke originates due to multiple reasons appearing after manipulation of different structures during surgery *e.g.*, intracardiac thrombi, susceptible atheroma in the aortic arch region, large arties laden with the atherosclerotic lacerations [79, 80]. Furthermore, there are also possibilities of watershed infarction due to intraoperative hypotension in patients that have been characterized with the pre-existent steno-occlusive disease (SOD) of the large artery [81].

Different studies have signified the greater propensity of females towards stroke as a post-surgical complication of stroke [82], while other studies consider both genders to be at risk in an equal manner [83, 84]. Hogue et al. [83] in single as well as multicentre studies, found the higher vulnerability of females than males towards post-surgical stroke and stroke-related mortality. While Koch et al. [85] found the equal vulnerability of both sexes with analogous risk profiles on the basis of propensity-based analysis. Gender differences have also been carefully studied for comprehension of the risk factors of stroke, *e.g.*, craniocervical and ascending aortic atherosclerosis in the CABG patients having age greater than 60 years. Unlike the conventional results, the analysis expressed the greater vulnerability of males towards stroke incidence expressed from CS, PVD, and severe aortic atherosclerosis. However, there is a profound similarity between the cerebral and cognitive impairments in the case of both sexes [86]. The significant polemical ability exists upon the greater propensity of female towards stroke incidence but older age and comorbidity existence has been accepted for their influential role [82]. Furthermore, the previous history of stroke in both sexes leads to the incidence of stroke after CABG surgery; however, craniocervical and aortic atherosclerosis are good predictors of post-surgical stroke [83, 84]. There is a lack of data existing on the studies based on gender differences prior to cerebral infarction. Among different risk factors of post-surgical strokes, older age >70 years has been reported to be one of the prominent risk factors [87]. Older age patients are more vulnerable to the incidence of stroke following CABG surgery due to restrained or serious aortic atherosclerosis [88, 89]. Nevertheless, other studies also point out the incidence of stroke in all ages leading to the death of the American Indian (AI) [90]. The comparison of AI individuals with the US expressed the young age deaths of AIs. Furthermore, other risk factors were also enhanced in the AIs [91]. Considerable variation existed within the AI population in terms of CAD-based mortality with the highest proportion

of the population residing in Dakota, Wisconsin, and Michigan. Apart from age as a risk factor, the ethnic differences also mark the incidence of post-surgical stroke in AIs [92, 93]. Highest mortality of 4.5% has been reported for AIs in comparison to other ethnic groups [94]. A study by Anderson et al. [95] explained the propensity of the younger individuals, most likely females having the atherosclerotic disease and augmented rated of diabetes dependent upon insulin and active tobacco users (Fig. 9). An investigative duration of 5 years after CABG surgery revealed a similar risk of both groups towards the development of stroke.

CAD patients undergoing CABG surgery are often detected with the CAS [96]. Concomitant CAS and ischemic CAD have been escalating around the globe due to urbanization. CAS has been marked as a strong and high-risk factor for post-surgical ischaemic cerebral discomfort. The risk of post-surgical stroke can be effectively reduced by the utilization of the routine duplex screening for the identification of significant CAS and consequently causing a depression in the risk of stroke [97]. ⩾50% are likely to develop CAS after CABG and thus leading to stroke [98]. Out of this ⩾50% stenosis, approximately 12.8% to 22% of the patients are residing in western countries [99].

Abbreviations

AF	Atrial fibrillation
AI	American Indian
AIS	Acute ischemic stroke
AMI	Acute myocardial infarction
anOPCAB	Aortic no-touch off-pump technique
CABG	Coronary artery bypass graft
CAD	coronary artery disease
CART	Coronary artery revascularization therapies
CAS	carotid artery stenting
CCSR	Chinese cardiac surgery registry
CEA	Carotid endarterectomy
CPB	Cardiopulmonary bypass
CS	Carotid stenosis
CTS	Cardiothoracic surgical
ES	Evaluation systems
EuroSCORE	European system for cardiac operative risk evaluation
HF	Heart failure
IAS	Arterial steno-occlusive lesion
IVS	Isolated valve surgery
LAA	Left atrial appendage
LM	Left main
LOS	Length of stays
LVEF	Left ventricular ejection fraction
LVO	Large-vessel occlusion
MI	Myocardial infarction
MRI/A	Magnetic resonance imaging/angiography
OP-CAB	Off-pump coronary artery bypass
PA-CAB	Port-access coronary artery bypass
PAD	Peripheral artery disease
PCI	Percutaneous coronary intervention
POC	Postoperative cognitive dysfunction
PVD	Peripheral vascular disease
RCT	Randomized control trials
RES	Risk evaluation systems
SinoSCORE	Sino system for coronary operative risk evaluation
SOD	Steno-occlusive disease
STS	Society of thoracic surgeons
TAVR	Trans-catheter aortic valve replacement

Competing interests

The authors declare that they have no competing interests

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