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Retrospective Review on the Assessment of Long- and Short-Term Complications Associated with Coronary Artery Bypass Grafting

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Abstract

There is no retrospective review reported analyzing the risks and complications associated with the coronary artery bypass graft (CABG) surgery. To determine the significant risk factors for CABG surgery and to determine the incidence of various post-operative short- and long-term complications of CABG, MEDLINE, NHS Evidence and Web of Science databases were searched in a systematic way. An effort was made to review the 2015- to date researches but no date limits were imposed. Furthermore, a total of 9,704 research articles were identified dealing with CABG surgery on the initial bases; however, the current review has been restricted to 176 articles on the basis of relevancy towards the investigated topic. There was no national or international protocol identified for the distinctive relationship between CABG surgery and the incidence of various commodities, particularly atrial fibrillation, stroke, renal failure chronic ischemia, respiratory complications and diabetes. The critical analysis of different strategies aimed at the prevention of post-operative incidence of diseases suggested the careful evaluation of each method prior to surgery. CABG surgery done on patients with the previous history of different comorbidities gave rise to the worst health quality within a short time after surgery. Such ailments not only induced the long- and short-term complications among patients but also extended the hospital admissions and readmissions that influenced the economic status of the patient as well imposed a heavy burden on the health care resources of the hospitals.

Introduction

Cardiac patients having higher disease severity have been preferentially handled with coronary artery bypass grafting (CABG) for the last half-century as a major mode of revascularization. CABG is often preferred over other treatment options, particularly in patients suffering from Multi-vessel coronary artery disease (CAD). CABG has been known for alleviating the mortality rates in addition to the prevention of myocardial infarction (MI) [1]. Approximately 2 million cardiac operations are being done on a global scale on an annual basis [2]. The first ever CABG surgery was endeavored by Dr. Rene Favaloro on May 1967. Dr. Favaloro operated the interpolated saphenous vein graft (SVG) and subsequently employed bypass surgery towards the contiguous aorta. This breakthrough in form of routinely done technique, *i.e*., CABG developed by Dr. Favaloro was envisaged as a transformative therapy for CAD patients with an elevated factor for reproducibility and lifesaving. To date, CABG has been done globally in a sustained manner. Thus, many renowned scientists have expressed their will in referring Dr. Favaloro as the "father" of CABG in the clinical arena [3]. Though, the historical aspect of CABG has never been free from analytical evaluation in terms of quality and medical efficacy in addition to the diminishing compensation and challenges associated with the percutaneous coronary intercession. Furthermore, there have been commendable advancements in the CABG technique irrespective of causing any kind of disruption in clinical prospects. Thus, CABG has been expected to be celebrated for a further 50 years unless and until there are any other miraculous therapies developed for curing reverse coronary atherosclerosis [4].

Major goals associated with CABG are the maximization of the survival rates in the long term for CAD patients, symptom mitigation and better economic value for patients and societal setups for socioeconomic gains. The survival of CABG operated patients is functioned by the complex role played by the populous facets and several risk factors [5] in addition to the decisions made by the surgeon prior to surgery. Some of the preoperative surgical decisions involve selection of the specific conduit for grafting [6], perfection in revascularization [7], managerial strategies adopted for blood [8] and finally the decision of selecting either on the pump or off-pump procedure. There have been an immense data representing the multiple arterial CABG (MABG) expressing superiority over the conventional CABG, *i.e*., left internal thoracic artery (LITA)-based CABG (SABG) that accounts for up to 90% of the majority of CABG undergone patients. However, CABG remains the basic gold-standard technique for multivessel CAD due to its outstanding results for left internal mammary artery (LIMA) in case of left anterior descending (LAD) artery revascularization [9, 10].

Despite the developmental advancements done for the improvement of clinical aspects of CABG, there has been a number of challenges associated with the CABG surgery. Such challenges are exhibited in the form of different risk factors and both short- and long-term complications. Though CABG has always remained the standardized protocol for survival rate enhancement of CAD patients, yet different risks involved are being investigated in different parts of the world. However, no retrospective review has been reported for CABG associated risk factors and complications to date either at a regional or global scale. Thus, the current review has undertaken the task of filling this gap by meticulously reviewing different complications associated with CABG. The review is envisaged to provide the cardio surgeons and young scientists with comprehensive details on CABG. Current work can be extended by different surgeons in the cardiology field by the addition of their strategies for sustained management of CABG undergoing CAD patients.

Methods

Literature review

For the assessment of the major risk factors and complications associated with CABG surgery, voluminous investigations were done employing the MEDLINE, NHS Evidence and Web of Science databases. In this regard, all cases involving CABG on a global scale were scrupulously studied and the searching standard was varied as ["Coronary artery bypass graft" OR "CABG" OR "risk factors of CABG" OR "short term complications of CABG" OR "long term complications of CABG"] either in title or/and abstract. Primarily articles in English were chosen and reviewed. An effort was made to review the latest researches, *i.e*., 2015- to date but no date limits were imposed. Furthermore, a total of 11,704 research articles were identified dealing with CABG surgery on the initial bases; however, the current review has been restricted to ≈200 articles on the basis of relevancy towards the investigated topic. Research article duplicate versions and false positives were omitted.

Results

Risk factors

Cardiac surgeons have agreed upon the effectiveness of CABG surgery in cases of coronary revascularization. Nevertheless, the results of CABG surgery have not achieved a satisfactory level in patients exhibiting high-risk medical history, *i.e.*, senility, malfunctioning of the left ventricle, diffused CAD, etc. [11]. Due to the provisioning of symptomatic relaxation and prevention of ischemic entanglements, CABG surgery has been used widely but the fact of complexity in triggering the consequential organ failures and physiological alterations is equally considerable [12]. For instance, it has been proved that there is an overall reduction in the complication incidence after CABG surgery; nonetheless, the cases reporting the incidence of postoperative stroke are marked with consistency in up to 0.8 – 6% of CAD patients having undergone CABG surgery. One of the decisive factors in this regard is that in cardiac occlusion or stenosis are being bypassed by venous or arterial grafts. There is a routine utilization of the cardioplegia, *i.e.*, temporary cardiac arrest initiation in which there is a coupling between the patient's heart and cardiopulmonary bypass via median sternotomy [13]. Around 21% of mortality has been reported for CABG postoperative stroke requiring approximately 25 days for the surviving patients. CABG postoperative stroke needs costly treatment.

Previous studies have confirmed that the CAD patient who have undergone CABG surgery, having any complications after surgery are marked by up to 1.4- and 8-fold augmentation in the mortality rate in comparison to the patients who do not express any complications [14]. An augmented disease incidence, *e.g.*, kidney and cardiac failure, hypertension, diabetes mellitus, etc. and aging populations points towards the need for surgical procedures [15-17]. Another study has also defined the incidence of elevated risk of peri-operative myocardial injury (PMI) and myocardial infarction (MI) exhibiting worst medical results after CABG surgery. It has also been predicted that by 2030, there would be 8 million CAD patients as a result of long-term materialization of CAD, malfunctioning of the left ventricle and cardiac failures. This fact is also associated with huge societal influence for the loss of such greater lives [18].

A myriad of risk factors has been reported for CABG surgery, depending upon the surgeon's expertise, patient's physiological state, and socioeconomic status. Among all risks, there is an increased risk of bleeding from the location where graft has been attached, for that reason, 30% of patients are known for expressing the need for blood transfusion. Furthermore, there can be irregular heart rhythms which can exhibit in their contribution towards blood clot formation consequently causing co-morbidities like cardiac failure, stroke and breathing ailments. Very less percentage of patients, *i.e.*, 1% have shown the risk infection at the site which has been incised for surgery. Other post-operative risks associated with CABG surgery can be renal failure, loss of normal cerebral functioning, post-pericardiotomy syndrome and ultimately death. Risk following CABG surgery has been predicted for 1-month mortality and is currently being researched at an exponential rate. There are a number of predictive models (Table 1) [20-38] used by cardiac surgeons [19] but the frequently used models for cardiac surgery are Euroscore system and the Society of Thoracic Surgeons (STS) 2008 Cardiac Surgery Risk Model.

Table 1 Risk stratification models used by Nilsson et al. [19] for the comparison of preoperative risks of the coronary artery bypass graft.

Sr. No.	Risk Model	Reference
1.	Amphiascore	Huijskes et al. [20]
2.	Cabdeal	Kurki et al. [21]
3.	Claeveland clinic	Higgins et al. [22]
4.	EuroSCORE (add.)	Nashef et al. [23]
5.	EuroSCORE (log.)	Roques et al. [24]
6.	French score	Roques et al. [25]
7.	Magovern	Magovern et al. [26]
8.	New York State	Coronary artery bypass surgery in New York State [27]
9.	Northern New England	Eagle et al. [28]
10.	Ontario	Tu et al. [29]
11.	Parsonnet	Parsonnet et al. [30]
12.	Parsonnet modified	Gabrielle et al. [31]
13.	Pons	Pons et al. [32]
14.	Toronto	Ivanov et al. [33]
15.	Toronto modified	Ivanov et al. [34]
16.	Tremblay	Tremblay et al. [35]
17.	Tuman	Turnan et al. [36]
18.	UK national score	Bridgewater et al. [37]
19.	Veterans Affairs	Grover et al. [38]

These models evaluate the CABG post-operative risks based on different variables such as age factor, history of myocardial infarction, peripheral vascular disease (PVD), kidney failure, hemodynamic state and ejection fraction. The STS model predicts the CABG post-operative risk up to 78% based on the variance of age, surgical intelligence, preoperative standing,

creatinine status, dialytic condition, shock, ejection failure and chronic lung disease. Around 30-40% of patients undergoing CABG, that also experience post-operative atrial fibrillation (POAF) have been known for an augmented risk of MI [39], post-operative stroke [39-41], persistent congestive heart failure [39], ventricular arrhythmias, kidney malfunctioning or failure [40, 42], stomach ailments [41] and alterations in memory. Some of the significant risk factors have been explained in the following section:

Bleeding risk

Patients undergoing CABG surgery are often given red blood cells (RBC) transfusion either at the time of surgery or later on. Blood transfusion is regarded as a life savior and important factor for improvement of heart function in CAD patients. Despite all benefits associated with the RBC transfusions, there are some serious risks, *e.g.*, it can give rise to the infectious agent transferal to the patient, the patient might express allergic reactions homologous RBC transfusion and more notably patients are vulnerable to elevated bacterial infection risk. The relationship between RBC transfusion and commencement of bacterial infection after CABG surgery has been reported. Researchers have also assessed the independence of the RBC transfusion and bacterial infections initiation. The results confirmed the augmented bacterial infections originating as the blood transfusion was done due to an increment in the RBC units [43].

Another postoperative risk of CABG surgery is platelet dysfunction. In order to reduce such risk, surgeons have also used clopidogrel for treating bleeding complications after CABG. However, the combined role of clopidogrel and aspirin needs further investigation for causing alterations in packed RBC and cryoprecipitate transfusions following CABG [44]. Furthermore, there is considerable evidence on the efficacy of dual antiplatelet therapy (DAPT) in comparison to the single APT for improvements in the venous grafting after CABG surgery. Nevertheless, there are some confusions existing regarding the use of DAPT following CABG may be associated with an enhancement in the bleeding risk, especially in the start of the CABG surgery post-operative duration. The use of DAPT has been known for safety in patients that undergo CABG surgery.

Incision site infections

Rigorous efforts have been done for medical care and improvement in the medical quality for achieving alleviation in the incidence of infections occurring after surgeries. Despite such advancements, 5% of the patients have been reported to express severe infections following cardiac surgery [45]. Researchers have also investigated the relationship between risk factors and the occurrence of the secondary surgical-site infection (SSI) following CABG surgery. The morbidity has been influenced by secondary SSI after CABG surgery. Secondary SSI has been found to be occurring right after the patient has been discharged from hospital and possesses a close association between saphenous vein grafting (SVG), increased body mass and RBC transfusions. Thus, patients exhibiting secondary SSI are often marked by longer stays and readmissions [46]. Investigations in this regard confirm 1-4% of the CABG undergone patients expressing SSI of the saphenous vein graft suffer from significant morbidity and operational costs [47-49].

Some cases also reported the loss of limb associated with SSI [49]. Though different studies have emphasized the saphenous vein harvesting, studies regarding infection being the primary endpoint are scarce. Neither has been the patients obtained follow-ups after one month, thus such studies are mostly retrospective [48, 50, 51]. There is a direct link between the number of surgeries and incidence of SSI, as the number of surgeries has increased, cases regarding SSI have also been exponential [52]. SSI as CABG surgery post-operative risk has significant implications on the economy and rates of morbidity and mortality [53]. Patients undergoing CABG surgery with multiple complicated comorbidities have expressed rising trend in Sternal infections [54]. Researchers have also emphasized on the use of ECG lead wires aimed at use for only one patient. Such a strategy might nullify the chances of SSI due to cross-contamination in comparison to the utilization of reusable ECG wires [55].

Breathing risks

Patients undergoing CABG surgery are also characterized to have developed several respiratory complications. They are often treated by utilization of extracorporeal circulation that subsequently gives rise to lung injury. Cardiac surgeons have favored the post-operative respiratory response of the patients who have undergone off-pump coronary artery bypass grafting (OPCABG) in comparison to on-pump coronary artery bypass grafting (ONCABG) [56]. Furthermore, patients have also complained about the occurrence of pernicious ventricular arrhythmias, which can be attributed to the irregular cardiac repolarization following CABG surgery.

However, in the non-surgical patients, the extended cardiac repolarization can also cause sleep-disordered breathing (SDB). Work has been done with CABG surgery undergone patients that either expressed or did not express SDB symptoms. Results have explained the utmost possibility of the contribution of SDB in increasing the ventricular arrhythmias following CABG surgery [57]. Postoperative cardiac arrhythmias are often developed and influenced by various risk factors, *e.g*., old age, male sex, cardiac disease and obesity [58, 59]. Studies have confirmed the independence and influence of the SDB on postoperative morbidity or mortality but had a pronounced impact in case of sepsis and pneumonia following CABG surgery [60].

Graft failures

CABG surgery has also been debated for graft failures. Though, there has been a considerable reduction in the death rate of CAD patients who underwent CABG surgery. But the recent studies have also confirmed the failure of bypass grafts, which gives rise to an elevated risk of MI and subsequent death. In order to resolve this issue, cardiac surgeons have come up with the utilization of rivaroxaban. They also suggested the use of rivaroxaban and aspirin be used collectively or in solitary for efficient deterrence of graft failure [61]. Graft failure leading to the unsuccessful CABG surgery, also increases the risk of sudden cardiac death (SCD) [62]. Furthermore, patients who have undergone CABG surgery and have extended intubation durations, *i.e*., 424 or 436 h following the surgery has been represented as an independent risk factor. These risk factors must be defined for clinical clarity and for adaptation of different strategies for the enhancement of care of STICH-like patients [63].

Postoperative complications

Patients that underwent CABG surgeries have been documented with several complications that needs a meticulous consideration of cardiac surgeons for sustained cardiac results (Table 2) [64 – 83]. Studies have confirmed the actuarial estimated survival rate following CABG surgery to be 92.0% at 45 months (n= 250). Among those, 13 dead patients were characterized for having different diseases, *i.e*., cerebrovascular failure, cancer, multisystem failure, pneumonia and cardiac failure [84]. In another study, the long-term survival rate of the CABG surgery undergone patients was evaluated (n=110) in which the survival rate was estimated to be 95% at 5 years and 92% at 10 years [85]. In this regard, various predictive models have been designed for short-term complications following CABG, and considerable efforts have also been made for the proposition of such models to predict the long-term complications and chances of survival. In fact, most of the surgical processes aimed at cardiac restoration are marked by causing an enhancement in the long-term survival and improvement in different symptoms. At the same time, these surgical protocols also aim at the reduction in the probable risk of morbidity and mortality in short- term [86]. In comparison with percutaneous coronary interventions (PCI), no controversies regarding CABG surgery induced survival rates has been documented [87-91].

Despite goals made for the maximization of long-term outcomes, the complications arising after CABG surgery are quite pronounced. In a combined surgical protocol, CABG and coronary endarterectomy (CE) have been shown to enhance 1-month post-operative mortality and incidence of MI, low output syndrome (LOS), ventricular tachycardia (VT) and kidney dysfunction [92]. The incidence of long-term and short-term complications has especially been more significant in patients with high-risk profiles and left anterior descending artery (LAD) diffused disease [93]. Other competitive techniques, *i.e*., hybrid coronary revascularization (HCR) and conventional CABG surgery have shown an improvement in the short-term outcomes but they also increased the patient's demand for repeat revascularization [94]. CABG with left internal mammary artery (LIMA) to the left anterior descending artery (LAD) has also been found for conferring survival advantages [94]. Following sections has briefly explained the recent advances regarding CABG surgery post-operative short- and long-term complications:

Atrial fibrillation

When there is an irregular unpremeditated release of calcium from the sarcoplasmic reticulum, this consequently causes an augmentation in the occurrence of the intrinsic Na-Ca exchange currents (ITI) contributing towards the incidence of the atrial fibrillation (AF). The occurrence of the AF due to significantly adjusted calcium homeostasis is influenced by the variety of the clinical factors. But unfortunately, there is no larger population-based evidence for this hypothesis due to some limitations, *i.e*. obtaining extremely minor yield and the inability for the accomplishment of successful experiments done on the atrial myocytes obtained from human specimens [95]. Around, 20-40% of the patients who have undergone CABG surgery are known for the

development of AF. In this regard, patients' recognition with higher vulnerability towards arrhythmia can be beneficial for targeting specifically those patients who have benefited from prophylactic therapy. Several studies have investigated the relationship between the incidence of AF following CABG surgery and the utilization of the expectedly distinct signal-averaged P-wave duration (SAPD) cutoff. Such studies were specifically aimed at the determination of postoperative AF incidence. The results are clearly in favor of the fact that development of AF following CABG surgery is a collective factor of the extended SAPD, older age and male sex in the patients suffering from CAD [96].

Most prominent risk factor for POAF is age, which has also been consistently substantiated by various researchers as well [97-102]. Risk factor for POAF after CABG surgery have also been analyzed via Bayesian analysis for differentiation of the test importance and effect level [103]. Other factors that can possibly elevate the chances for the incidence of POAF can be male sex, obesity, high blood pressure, heart/kidney failure, high cholesterol level, diabetes mellitus, smoking, MI history, obstructive pulmonary ailment, echocardiographic issues, and peripheral artery ailment [97-102, 104]. Furthermore, a patient who discontinues treatments is also known for being at an increased risk of PAOF incidence.

Post-operative AF (POAF) has been known as the most frequently occurring complication of CABG surgery. CAD patients who develop symptoms of POAF are often given extended hospitalization, readmittance to the ICU, an elevated healthcare resource utilization and can suffer from fluxionary cardiac failure, stroke. Cardiac surgeons around the globe have fastened their efforts in prioritizing the reduction of morbidity and mortality by correct identification of the preoperative risk factors, medical models aimed at prediction and prophylactic procedures. One of the efforts done in this regard is the utilization of beta blockers for better control of the ventricular and atrial-based arrhythmias in addition to the simultaneous consumption of myocardial oxygen and also an ischemic burden.

Treatment of the myocardial cells with n-3 polyunsaturated fatty acids (PUFA) possessing antiarrhythmic characteristics have also been reported. The oral administration of PUFA has been found to be reducing the rate of AF following CABG surgery. Furthermore, if PUFA is intravenously injected in the patient prior to CABG surgery, patients will have to stay for a short duration in the hospital. Thus, the intravenous infusion of PUFA has been strongly recommended for CABG surgery undergoing patients [105]. All-embracing melioration has been achieved for about 6 months after CABG surgery by the successful use of the beta blockade prior to the operation. Patients having left main coronary artery disease (LMCAD) were revascularized in an EXCEL trial and results expressed that new-onset atrial fibrillation (NOAF) was more frequent in comparison to PCI, in which the chances of NOAF are rare in terms of incidence. NOAF subsequently gave rise to stroke and death in the CABG surgery undergone patients. An emphasis must be given to the exploration of the determination of prophylactic procedures for the prevention or treatment of the AF might prove efficient in LMCAD patients who are being treated with the CABG surgery [106]. Additionally, the CABG candidate patients can be effectively prevented from the incidence of POAF by utilization of the combination as prophylaxis which will ultimately reduce the operational costs, mortality rate and side effects after CABG surgery. Such POAF incidence alleviation can either be achieved through the use of metoral and magnesium, but metoral has been found to be more effective than Mg. However, further better results can be obtained by the addition of both. Cardiac surgeons around the globe have also been suggested to investigate the efficacy level of the metoral + Mg and metoral + reinforcing factors, *e.g.*, statins and saturated fatty acids [107]. Another study confirms 22% POAF risk alleviation in the CABG treated patients by the utilization of Warfarin. This study is also indicative of the occurrence of the embolic events leading to death, particularly in freshly diagnosed POAF [108].

Stroke

Patients who have undergone CABG surgery and developed POAF are equally at an elevated risk for main cardiovascular events, especially stroke and mortality [109]. Stroke after CABG surgery has been considered as one of the most damaging complications due to its contribution to higher mortality and morbidity. Disfigured life quality and having been admitted to the secondary centers for care has been yet another damaging aspect of stroke as a postoperative complication of CABG. Studies have confirmed the independence of the thrombocytopenia (moderate-severe) and stroke in addition to the timings of incidence after the CABG surgery [110]. In contrast to CABG surgery, patients were needed to stay 8 or fewer days in the case of PCI. However, this decrease in stay timings and stroke

Table 2 Short- and long-term complications reported in year 2018 for patients that underwent coronary artery bypass graft (CABG) surgery.

Sr. No.	Study	Study design	Duration	Major findings
1	Ríos et al. [64] (n=36)	Retrospective study with bilateral internal mammary arteries (BIMA)	Jan. 2012 to Dec., 2015	CABG surgery in combination with BIMA signified the procedure to be safe and ensured the alleviated mortality rates with essential short-term cardiac events.
2	Sun et al. [65] (n=68,836)	Retrospective cohort study	Oct. 1, 2008, and Mar. 31, 2015	Heart failure (HF) with preserved ejection fraction (pEF) was prevalent in females. HF proved to be a better prognosticator in comparison to ejection fraction. Follow-ups after CABG surgery must involve both genders.
3	Bishawi et al. [66] (n= 2, 203)	Randomized on/off bypass (ROOBY)	2002 to 2007	CABG surgery underwent patients had the worst health-related quality of life (HRQL) following. Clinicians must consider the better use of pre-CABG counseling in patients to make them aware of the possible HRQL ameliorations.
4	Raja et al. [67] (n=668)	Invasive direct coronary artery bypass (MIDCAB)	Feb. 1996 to Oct. 2017	MIDCAB was concluded to be an efficacious procedure for left anterior descending artery (LAD) grafting but there is no evidence of the suitability of invasive approach in comparison to the full sternotomy
5	Smart et al. [68] (n= 8, 145)	Systematic analysis	-	Despite the unclear clinical influence, statistical data shows the superiority of the on-pump CABG surgery.
6	Butt et al. [69] (n= 2, 108)	Cohort study	Jan. 1, 2000 to June 30, 2015	The fresh commencement of the postoperative atrial fibrillation (POAF) in patients that have undergone CABG is attributed to the low-level long-term risk of thromboembolism in comparison to patients with nonvalvular atrial fibrillation (NVAF).
7	Benedetto et al. [70] (n=3, 102)	Post hoc arterial revascularization trial (ART) analysis	2004 to 2007	The risk of early and late mortality was considerably increased due to aprotinin.
8	Royse et al. [71] (n=51, 113)	Patient data extraction	2001–2013	There is a factor of independence between the utilization of the saphenous vein graft intervention and CABG surgery.
9	Kilpin et al. [72] (n= 34,961)	Risk modelling	2001-2017	Risk modeling successfully predicted the postoperative long-term mortality associated with CABG surgery. Utilized risk models did not produce good results in the case of Australia.
10	Schwann et al. [73] (n= 8,807)	Non-salvage CABG	1994–2011	Higher incidence of the cerebrovascular and cardiovascular mortality in the intermediate term gives rise to POAF.
11	Yousif et al. [74] (n= 11, 374)	Randomized control trials metal-analysis	Jan. 1, 2000 and Aug. 1, 2016	Despite the higher financial resources spent on extended hospitalization, there is an alleviation in the risk of revascularization in case of on-pump CABG.
112	Tantawy et al. [75] (n= 2, 180)	Retrospective medical record review	June 2006 to May 2013	Statistical evaluation of the blood transfusion given to patients who have undergone CABG surgery was done expressing the non-significance of results in 3 years. Further investigations must be done to explore the benefit of blood transfusions to the patients.
13	Meneguzzi et al. [76] (n= 8, 294)	Prospectively compiled database-based investigation	3 Jan. 2005 and 31 Dec. 2011	The rate of bleeding and need for blood transfusion is significantly increased upon the late discontinuation of aspirin.
14	Nonaka et al. [77] (n= 48, 177)	Reimbursement data study	July 2008 and Mar. 2016	PCI and CABG surgery were not markedly different in terms of survival rate but the rate of MI incidence after PCI in comparison to CABG surgery was significantly higher.
15	Klinkhammer [78] (n= 337)	Retrospective review	Aug. 10, 2012 to Nov. 15, 2016	Patient history depicted no difference in the survival rate for CABG and transcatheter aortic valve replacement (TAVR).
16	Beck et al. [79] (n= 353)	Retrospective review	Jan. 1, 2010, and Nov. 11, 2015	6% of the patients, which were operated with CABG has an incidental pulmonary embolism (PE) and in the majority of the cases, there was a spontaneous resolution without any occurrence of the anticoagulation.
17	Head et al. [80] (n= 11, 518)	Systematic review	Inception to July 19, 2017	CABG surgery is preferable in terms of mortality benefit over PCI particularly in patients suffering from diabetes and elevated coronary complications.
18	Tran et al. [81] (n= 40, 083)	Retrospective cohort study	2008 and 2015	Significant weakness is prevalent in the patients after CABG surgery and has an independent association with the long-term mortality. There is an indirect proportionality between age and weakness associated with death.
19	Filardo et al. [82] (n= 11, 239)	Clinical data in-hospital ECG/telemetry monitoring	2002 to 2010	~800 000 patients undergo CABG on an annual basis on a global scale, out of which >264 000 are likely to develop postoperative atrial fibrillation. Better management and efficacious prophylaxis are required on an urgent basis for a reduction in the worst outcomes.
20	Beller et al. [83] (n= 1,272)	Logistic regression assessment	2002-2016	There is a positive correlation between the troponin utilization prior to surgery and worst results but through the adjustment of risk, the predictive value of the biomarker in the short term can be eliminated.

incidence risk gave rise to the need for repeated revascularization thus challenging the defected favorability of PCI over CABG surgery [111]. However, the overall procedure inclusive of the hospital stay costs, CABG surgery cannot excel PCI for minor stroke risk and financial benefits.

Stroke incidence following CABG surgery can be attributed to the hypotension/ hypoperfusion prior to the surgery and thromboembolism. Additionally, the increased vulnerability of fewer patients in comparison to others as a candidate for CABG surgery can be an increased age factor, carotid artery disease, recent MI, previous history of the cerebrovascular event and aortoiliac arterial disease. In fact, the longer hospital stays, higher mortality rates and other relevant complications are all due to stroke following CABG surgery [112]. Reports have also successfully identified the patients with the elevated risk of developing perioperative stroke for decreasing the other complications after CABG [113]. A considerably significant neurological insufficiency that appears within the first 30 days after CABG surgery is referred to as perioperative stroke and has been considered a very damaging complication of CABG surgery. Perioperative stroke increases the rate of mortality and morbidity up to 5-folds and acts as a significant factor for draining the hospital resources [114, 115]. The percentage of patients undergoing CABG for perioperative stroke incidence is 0.8-5.2% [116-119]. Since completely different pathophysiological mechanisms govern the incidence of perioperative and delayed strokes, thus, a clear distinction between both must be achieved. Only three studies have given an account of this differentiation [120, 121] by reporting the incidence of earlier strokes to be 0% [122] and 0.1% [120].

There have been no advancements for a reduction in postoperative stroke for the last 2 decades despite advancements in the patient care facilities, surgical procedures and equipment for cardiopulmonary bypass [123]. Though recently, the considerable minimization has been achieved in risk of stroke by using an aortic (aortic no-touch) OPCAB (anOPCAB) procedure [124]. Patients with older age, congestive cardiac failure and previous history of stroke aggravate the post-operative CABG surgery outcomes [125]. Studies have confirmed the efficacy of the mechanical thrombectomy driven recanalization in comparison fibrinolytic compounds drove recanalization [126].

Renal collapse

Renal failure remains another significant postoperative complication. Studies have reported up to 0.3-29.7% of the incidence of renal failure in the specifically selected population [127, 128]. Around, 1.2-3% of the patients are also characterized for their need for renal replacement therapy (RRT), which is another contributing factor towards augmented mortality [129, 130, 131]. Generally, there is an increasing urge for remote ischemic preconditioning (RIPC) that is associated with the improved mitigation for the kidney ischemic reperfusion injury following CABG. This surgical procedure also acts as a prophylactic strategy for acute kidney injury (AKI) after CABG surgery [132]. Studies on the comparative analysis of AKI incidence after CABG and percutaneous coronary intervention (PCI) have confirmed the consistency in AKI occurrence in most cases [133]. Surprisingly, the incidence of AKI in CABG patients has been found to be increasingly causing higher mortality with the passage of time.

Despite contemporary advancements done in the comprehension of etiological and pathophysiological aspects of AKI following CABG surgery, no apparent alleviation has been observed in the frequency or mortality caused due to AKI [134]. Furthermore, the existence of conventional prophylactic procedures or AKI treatment is also scanty. Surgical specialists consider the development of efficacious prophylaxis, advance clinical results and less use of resources to be the solution in this regard [135]. Different risk factors have been associated with the incidence of AKI in CABG treated patients, *i.e*., old age, fluxionary cardiac failure, diabetes mellitus, surgical complications, emergency surgery need and chronic kidney disease (CKD) prior to surgery [134, 136, 137]. Furthermore, pathophysiological factors also equally contribute to AKI risk, *e.g*., alterations and disruptions in renal blood flow, embolism, inflammatory intermediaries and iodinated contrast exposure when the diagnostic angiography is being carried out [138, 139]. There is a close relationship between the frequencies at which AKI occurs and the foundational renal functionality, consequently, AKI is highly prevalent in patients suffering from severe CKD but patients with mild renal ailments are also at the risk of AKI development in comparison to those patients who are not characterized by renal ailments prior to CABG surgery. Furthermore, surgical specialists must consider the possibility of risk for AKI development prior to the selection of the cardiac revascularization procedures in addition to different ways that are aimed at prevention of AKI following

the revascularization. Cardiac surgeons have also confirmed the increasingly greater incidence of AKI and its trend is also incremental in direct proportion with augmenting CKD. CKD is often related to the cardiovascular mortality and morbidity rate inclusive of both short- and long-term complications.

Results of studies on haemodialysis done in the last stage of kidney failures have confirmed more than 20% incidence in the first year of treatment. Among them, half of the death toll is attributed to cardiovascular diseases (CVD) while 20% occurs due to acute MI. There has been a controversial aspect in comparison of the medical efficiency of PCI versus CABG; however, utilization of stents that are eluted with drugs and use of neoteric pharmacotherapeutics showed better results [140]. Recent studies have utilized N-acetylcysteine, vitamin C and selenium prior to the CABG surgery but it did not prevent kidney damage and the rate of morbidity or mortality associated with it [141]. Patients that are a candidate for CABG surgery must be prevented from AKI because 1 out of every 3 CAD patients is reported as the risk of death [142]. Additionally, there is the possible incidence of the renal hypoperfusion and hypothermia due to the blood flow in a non-pulsatile manner after cardiopulmonary bypass [143-145]. Particularly the vulnerability of the male gender in contrast to previously done research for the incidence of major cardiovascular events after CABG in female have also been reported for a male after 1 month and 1 year following the CABG surgery.

Diabetes

Diabetes is a lifelong condition of health and becomes a major risk factor for CAD. The recent estimations express that diabetes was prevalent in up to 382 million patients in 2013 and was predicted to be increased to 592 million patients by 2035 [146]. European medical records show the dependence on insulin on a global scale is increased by 3%, while 5% in Europe on a yearly basis [147]. CABG surgery is done on diabetic patients with a glucose level of 141–180 mg/dL and 100 and 140 mg/dL did not show any significant reductions in the perioperative complications. Reportedly 60-90% of patients who undergo cardiac surgeries have a previous history of diabetes in comparison to other non-diabetic patients [148, 149]. Different cohort studies have expressed the independence of diabetes as a risk factor mortality and morbidity following cardiac surgery [150, 151].

Diabetic patients have expressed worst results of surgical procedures in comparison to the non-diabetic patients, *e.g*., significantly elevated mortality, wound infection in the sternal region, kidney failure, strokes, extended hospital stays and large-scale use of hospital resources. Thus, the survival of diabetic patients in the long term is also alleviated because these patients are often known for increasingly higher occlusion of SVG after CABG surgery [152]. The failures in the vein grafting in diabetic patients majorly occurs due to thrombotic occlusion [153]. Studies have also focused on the use of the second antiplatelet agent as a therapeutic option, especially in diabetics, but bleeding risks and conclusion-based evidence should be kept in mind.

Respiratory complications

Patients meant for CABG surgery can also be characterized by an impaired respiratory function. Patients can have many weeks of respiratory problems due to the dysfunctionality of respiratory muscles and extended durations required for recovery and incidence of the physical deconditioning [154, 155]. Cardiac surgeons have also recommended the utilization of a short-term inspiratory muscle training (IMT) procedure based on aerobics and training regarding resistance development in a cardiac rehabilitation program (CRP) following CABG surgery. Such practice has considerably enhanced the strength of the respiratory and their functionality [156]. Alterations done in the respiratory function following CABG surgery can be attributed to the circulatory aspects that play an active role in the protein synthesis in muscles. Nonetheless, such correlative behavior is not an indication of the causality. Aetiologically, there are multifactorial aspects involved in the dysfunctionality of pulmonary muscles following the CABG surgery [157]. CABG undergone patients have expressed the previous history for the incidence of chronic obstructive pulmonary disease (COPD). Both cardiovascular diseases (CVD) and COPD are similar in sharing the risk factor of smoking. COPD can ultimately develop into atherosclerosis [158].

Coronary ischemia

Ischemia is another significant complication associated with CABG surgery. There have been consistent reports on the incidence of the MI due to cardiac enzymes releasing prior to the surgery. Such a devastating clinical condition can significantly increase mortality and morbidity following the CABG surgery [159-163]. Ischemic preconditioning is usually done on the CABG treated patients as an intervention involving one organ's (or tissue's) brief ischemia for the protection of the remotely present

organs for prevention of the sustainable ischemic occurrence though yet it is not clear that [164]. In the long run, this method is also considered inapplicable in reality and invasive because of cross-clamps the aorta [165].

Abbreviations

AKI	Acute kidney injury
ART	Arterial revascularization Trial
BIMA	Bilateral internal mammary arteries
CRP	Cardiac rehabilitation program
CVD	Cardiovascular diseases
CKD	Chronic kidney disease
COPD	Chronic obstructive pulmonary disease
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CE	Coronary endarterectomy
DAPT	Dual antiplatelet therapy
HRQL	Health-related quality of life
HF	Heart failure
IMT	Inspiratory muscle training
ITI	Intrinsic Na-Ca exchange currents (ITI)
MIDCAB	Invasive direct coronary artery bypass
LAD	Left anterior descending
LIMA	Left internal mammary artery
LITA	Left internal thoracic artery
LMCAD	Left main coronary artery disease
LOS	Low output syndrome
MABG	Multiple arterial CABG
MI	Myocardial infarction
PUFA	n-3 polyunsaturated fatty acids
NVAF	Nonvalvular Atrial Fibrillation
anOPCAB	Anaortic (aortic no-touch) OPCAB
OPCABG	Off-pump coronary artery bypass grafting
ONCABG	On-pump coronary artery bypass grafting
PCI	Percutaneous coronary interventions
PMI	Peri-operative myocardial injury
POAF	Post-operative atrial fibrillation
PE	Pulmonary embolism
ROOBY	Randomized on/off bypass
RBC	Red blood cells
RIPC	Remote ischemic preconditioning
RRT	Renal replacement therapy
SVG	Saphenous vein graft
SSI	Secondary surgical-site infection
SAPD	Signal-averaged P-wave duration
SDB	Sleep-disordered breathing
STS	Society of Thoracic Surgeons
SCD	Sudden cardiac death
NOAF	New-onset atrial fibrillation
TAVR	Transcatheter aortic valve replacement
VT	Ventricular tachycardia

Competing interests

The authors declare that they have no competing interests

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