Systematic Review

A systematic review on robotic coronary artery bypass graft surgery

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Background: Robotic-assisted coronary artery bypass graft surgery (CABG) has been performed over the past decade. Despite encouraging results from selected centres, there is a paucity of robust clinical data to establish its clinical safety and efficacy. The present systematic review aimed to identify all relevant clinical data on robotic CABG. The primary endpoint was perioperative mortality, and secondary endpoints included perioperative morbidities, anastomotic complications, and long-term survival.

Methods: Electronic searches were performed using three online databases from their dates of inception to 2016. Relevant studies fulfilling the predefined search criteria were categorized according to surgical techniques as (I) totally endoscopic coronary artery bypass without cardiopulmonary bypass (TECAB off-pump); (II) TECAB on-pump; and robotic-assisted mammary artery harvesting followed by minimally invasive direct coronary artery bypass (robotic MIDCAB).

Results: The present systematic review identified 44 studies that fulfilled the study selection criteria, including nine studies in the TECAB off-pump group and 16 studies in the robotic MIDCAB group. Statistical analysis reported a pooled mortality of 1.7% for the TECAB off-pump group and 1.0% for the robotic MIDCAB group. Intraoperative details such as the number and location of grafts performed, operative times and conversion rates, as well as postoperative secondary endpoints such as morbidities, anastomotic complications and long-term outcomes were also summarized for both techniques.

Conclusions: A number of technical, logistic and cost-related issues continue to hinder the popularization of the robotic CABG procedure. Current clinical evidence is limited by a lack of randomized controlled trials, heterogeneous definition of techniques and complications, as well as a lack of robust clinical follow-up with routine angiography. Nonetheless, the present systematic review reported acceptable perioperative mortality rates for selected patients at specialized centres. These results should be considered as a useful benchmark for future studies, until further data is reported in the form of randomized trials.

Keywords: Robotic surgery; coronary artery bypass graft surgery (CABG); systematic review

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Introduction

Coronary artery bypass graft surgery (CABG) remains the standard of treatment for selected patients with coronary artery disease (1). Significant long-term angiographic and clinical benefits of CABG have been attributed to the left internal mammary artery (LIMA)-to-left anterior descending artery (LAD) graft, with historical studies demonstrating survival benefits over long-term follow-up beyond 15-years (2,3). Histopathological studies have identified particular characteristics of the LIMA endothelium, such as fewer fenestrations, lower intercellular junction permeability, greater anti-thrombotic molecules and higher nitric oxide production, all of which make

LIMA more resistant to atherosclerosis compared to saphenous vein conduits (4). The superiority of the LIMA-to-LAD graft is one of the main indications for surgical revascularization in the current era of drug-eluting stents (5).

Over the past two decades, minimally invasive surgery has evolved to influence many surgical specialties, including both cardiac and thoracic surgery (6-8). Complex cardiac operations such as mitral valve surgery and CABG have been performed with safety and efficacy through smaller incisions compared to the conventional sternotomy approach (7). Since the 1990s, robotic systems have been developed to facilitate minimally invasive cardiac surgery. Historical operating systems such as the Automated Endoscopic System for Optical Positioning (AESOP) and the Zeus Robotic Surgical System have evolved to the current da Vinci Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA, USA), which was approved for use by the Food and Drug Administration (FDA) in 2000.

Despite encouraging reports from small retrospective institutional studies, there remains a paucity of robust clinical data on robotic-assisted CABG procedures. Heterogeneous classification of 'robotic CABG' techniques and non-standardized reporting of endpoints have further hindered any meaningful analysis of the existing literature. The current systematic review aimed to assess the clinical outcomes of robotic-assisted CABG procedures according to three defined surgical techniques: totally endoscopic coronary artery bypass without cardiopulmonary bypass (TECAB off-pump); TECAB with cardiopulmonary bypass (TECAB on-pump); and robotic-assisted LIMA harvesting followed by off-pump manual anastomosis of LIMA-to-LAD through minimally invasive direct coronary artery bypass (robotic MIDCAB). The primary endpoint was perioperative mortality, and secondary endpoints included perioperative morbidities, anastomotic complications and long-term survival.

Methods

Search strategy and study selection

Electronic searches were performed using Medline, EMBASE and Central Register of Controlled Trials from their dates of inception to January 2016. The search terms ("CABG" or "coronary artery bypass") and ("robotic OR robot") were combined as both keywords and MeSH terms. This was supplemented by manually searching the reference lists of key reviews and all potentially relevant studies. Two reviewers (S.V. and P.I.) independently screened the title and abstract of records identified in the search. Full-text publications were subsequently reviewed separately if either reviewer considered the manuscript as potentially eligible for inclusion. Disagreements regarding study selection were resolved by discussion and consensus.

Eligibility criteria

Selected studies included those reporting peri-operative mortality after robotically assisted CABG procedures. These studies were categorized according to surgical techniques as (I) TECAB off-pump; (II) TECAB on-pump; (III) robotic MIDCAB. Studies that reported a mixture of surgical techniques were included for statistical analysis only when separate datasets were reported for patients in each group. All publications were limited to those involving human subjects and written in English, and studies with fewer than ten patients were excluded. When duplicated studies with accumulating numbers of patients or increased lengths of follow-up were identified, only the most complete reports were included for assessment.

Surgical techniques

Following intubation with a dual-lumen endotracheal tube, the patient was positioned supine with the left side elevated to 30 degrees and the left arm remaining at the side. With selective ventilation of the right lung and carbon dioxide insufflation of the left pleural space, three ports were inserted into the left thorax to optimize visualization of the surgical field and to maximize the range of motion for the robotic arms. Exact positioning of the ports depended on the surgeon's preference, target vessels, and patient body habitus. The robotic-assisted LIMA harvest was then performed via the two working ports under endoscopic vision through the third port. Upon completion of LIMA harvest and systemic heparinization, occluding bulldog clamps were be applied to the proximal LIMA, prior to grafting through a totally endoscopic approach, including either TECAB on-pump or TECAB off-pump, or via a left anterior mini-thoracotomy by robotic MIDCAB.

On-pump TECAB

Cardiopulmonary bypass was typically established via femoral venous and femoral or axillary arterial cannulation. Aortic occlusion could be achieved by an endovascular occluding balloon, placed and inflated in the ascending aorta under transesophageal ultrasound guidance. Cardioplegia could be delivered directly into the aortic root through a distal channel in the endoballoon. Alternatively, an endoscopic trans-aortic clamp could be applied via a port site in the chest wall and antegrade cardioplegia delivered via an endoscopically-placed vent needle in the proximal ascending aorta.

Off-pump TECAB

Following conduit harvest and preparation, a fourth port was inserted in the left subcostal or subxiphoid plane for the insertion of tissue stabilizing devices. The da Vinci telemanipulation system has a range of Endowrist instruments, (Intuitive Surgical Services, Sunnyvale, CA, USA) including a tissue stabilizer that could be docked to and manipulated by the robotic system. Other endoscopic tissue stabilizers include the Octopus Stabilizer, the CTS system (CardioThoracic Systems Inc., Cupertino, CA, USA), or the Elite Endoscopic Stabilizer (Genzyme Surgical Products, Fall River, MA, USA). Positioning devices such as the Starfish NS (Medtronic Inc., Minneapolis, MN, USA) could be used to manipulate and position the heart for multi-vessel anastomosis.

Robotic MIDCAB

Following the harvest of the LIMA as described above, the robotic system was undocked and CO_2 insufflation ceased to allow the heart to return to its natural position. An endoscope was used to identify the intended site of anastomosis and a spinal needle could be inserted through the chest wall to identify the precise location for the mini-thoracotomy incision. Alternatively, the previous port sites could be extended directly. A soft tissue retractor was used to provide exposure through the interspace, and the anastomosis was performed using endoscopic tissue stabilizers and standard off-pump anastomotic techniques. To maintain a consistency of surgical techniques, only off-pump robotic MIDCAB studies were included for detailed statistical analysis in the present systematic review.

Statistical analysis

Baseline characteristics and operative details were presented as raw values (%), mean ± standard deviation or median unless otherwise indicated. Pooled values for clinical outcomes were calculated using DerSimonian-Laird random-effects model and reported with 95% confidence intervals (CI) (9). For all studies, overall survival referred to freedom from death of any cause, and was calculated from the time of surgery. All statistical analyses were performed using Comprehensive Meta-analysis v2.2 (Biostat Inc., Englewood, NJ, USA). All P values were two-sided, and values <0.05 were considered statistically significant.

Results

Using the predefined systematic search criteria, a total of 978 unique records were identified through the database and bibliographic searches, with one additional study identified through other sources. After exclusion of duplicated studies and 546 irrelevant articles based on abstracts and titles, 126 studies remained for full-text evaluation. Of these, 44 studies met the inclusion criteria, including nine studies in the TECAB off-pump group (10-18); two studies in the TECAB on-pump group (19,20); and 16 studies in the robotic MIDCAB group (10,21-33). One study provided separate data for both the TECAB off-pump and robotic MIDCAB groups, and was included for analysis in both groups (10). Eighteen additional studies reported on a mixture of different surgical techniques (18,34-53). A summary of the study selection process is presented in the PRISMA chart in *Figure 1*, and a summary of study characteristics is presented in *Table 1*.

All of the studies were observational studies, including clinical data on a total of 8,034 patients who underwent CABG. Twenty-one studies were excluded from the final analysis due to a mixed dataset for different surgical techniques (42-53) or use of cardiopulmonary bypass (36-41), or use of an outdated robotic system other than the da Vinci system (18,34,35). Of the patients who were included for statistical analysis in the selected studies on off-pump TECAB, on-pump TECAB and robotic MIDCAB, the mean age ranged from 58 to 67, and 51–88% of patients were male. The presence of hypertension, previous myocardial infarction (MI) and diabetes mellitus were reported in 50–92%, 7–56% and 13–51% of patients, respectively. Preoperative estimated left ventricular ejection fraction (LVEF) ranged from 48–63% across studies. A summary of baseline patient characteristics is presented in *Table 2*. The reported follow-up duration ranged from the peri-operative period to eight years, and 20 studies reported routine angiographic follow-up 1–96 months postoperatively by either angiography or computed tomography coronary angiography (CTCA).

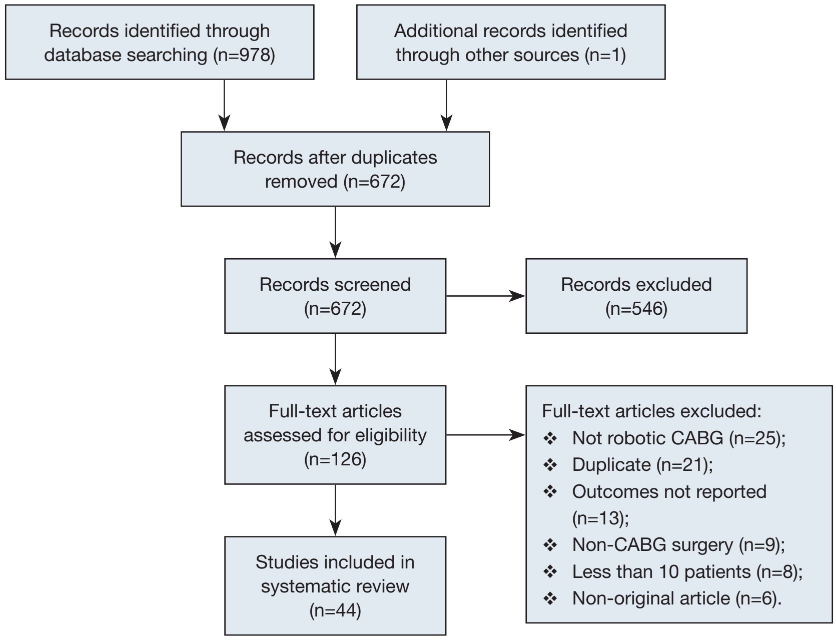

Figure 1 PRISMA chart summarizing the study selection process in the systematic review on robotic coronary artery bypass graft surgery.

Table 1 Study characteristics of relevant articles identified in the systematic review on robotic-assisted coronary artery bypass graft surgery

Technique	Study	Refs.	Year	Location	Study period	No. of patients
TECAB off pump	Yang *et al*.	(10)	2015	China	2007–2014	100
	Cheng *et al*.	(11)	2014	China	2007–2013	90
	Srivastava *et al*.	(12)	2012	USA	2008–2009	164
	Dhawan *et al*.	(13)	2012	USA	2007–2009	106
	Balkhy *et al*.	(14)	2011	USA	2008–2010	120
	Jegaden *et al*.	(15)	2011	France	2003–2008	59
	Srivastava *et al*.	(16)	2008	USA	2004–2005	108
	Fleck *et al*.	(17)	2005	Austria	2003–2005	14
	Boyd[Z] *et al*.	(18)	2002	Canada	1999–2002	84
TECAB on pump	Zaouter *et al*.	(19)	2015	France	2011–2014	38
	Argenziano *et al*.	(20)	2006	USA/Austria	2002–2004	85
MIDCAB off pump	Yang *et al*.	(10)	2015	China	2007–2014	140
	Daniel *et al*.	(21)	2014	USA	2008–2011	322
	Fujita *et al*.	(22)	2014	Japan	2004–2012	33
	Halkos *et al*.	(23)	2014	USA	2009–2012	307
	Leyvi[NR] *et al*.	(24)	2014	USA	2007–2012	150
	Sabashnikov[Z, A] *et al*.	(34)	2014	UK	2003–2013	236

Table 1 (*continued*)

Table 1 (*continued*)

Technique	Study	Refs.	Year	Location	Study period	No. of patients
MIDCAB off pump	Bayramoglu *et al*.	(25)	2013	Turkey	2004–2012	100
	Hemli *et al*.	(26)	2013	USA	2011–2012	77
	Liu[NR] *et al*.	(27)	2013	Taiwan	2005–2010	255
	Daniel *et al*.	(28)	2012	USA	2009–2012	256
	Poston *et al*.	(29)	2008	USA	NR	100
	Kiaii[Z, A] *et al*.	(35)	2006	Canada	2004–2009	100
	Srivastava *et al*.	(30)	2006	USA	2002–2004	148
	Turner *et al*.	(31)	2006	USA	2004–2005	70
	Subramanian *et al*.	(32)	2005	USA	2003–2004	30
	Mariani *et al*.	(33)	2002	Italy	2001–2002	24
TECAB (combined data)	Bonaros *et al*.	(36)	2013	USA/Austria	2001–2011	500
	Kappert *et al*.	(37)	2008	Germany	1999–2001	41
	de Cannière *et al*.	(38)	2007	Belgium/Germany	1998–2002	228
	Mishra *et al*.	(39)	2006	India	2002–2005	13
MIDCAB (combined data)	Kiani *et al*.	(40)	2012	USA	2008–2010	91
	Caynak *et al*.	(41)	2009	Turkey	2004–2007	196
Combined data	Cavallaro *et al*.	(42)	2015	USA	2008–2010	2,582
	Casula *et al*.	(43)	2014	UK	2002–2014	100
	Vainrub *et al*.	(44)	2014	USA	2012–2013	136
	Yang *et al*.	(45)	2013	China	2007–2012	200
	Anderson[NR] *et al*.	(46)	2012	USA	2008–2009	132
	Currie[NR] *et al*.	(47)	2012	Canada	1999–2003	82
	Hemli *et al*.	(48)	2012	USA	2010–2011	110
	Folliguet *et al*.	(49)	2010	France	2004–2008	56
	Loisance *et al*.	(50)	2005	France	2002–2003	110
	Novick[Z] *et al*.	(51)	2003	Canada	1999–2001	90
	Damiano[Z] *et al*.	(52)	2001	USA	NR	32
	Prasad[Z] *et al*.	(53)	2001	USA	NR	19

Studies including combined data were not analysed further in statistical analyses. TECAB, totally endoscopic coronary artery bypass; MIDCAB, minimally invasive direct coronary artery bypass; NR, not reported; Z, Zeus robotic system; A, automated endoscopic system for optimal positioning robotic system.

Intra-operative data

The mean number of grafts per CABG procedure ranged from 1–2.8 in all three surgical techniques. However, there was a trend of more grafts being performed in robotic MIDCAB procedures compared to TECAB procedures. The LIMA-to-LAD graft was performed in all patients who underwent on-pump or off-pump TECAB, apart from one study. Circumflex and right coronary artery (RCA)

Table 2 Baseline characteristics of patients who underwent robotic-assisted coronary artery bypass graft surgery

Technique	Study	Age	Male (%)	HTN (%)	Prior MI (%)	Diabetes (%)	LVEF (%)
TECAB off pump	Yang *et al*. (10)	58.7±8.6	84	50	20	26	62.8±5.1
	Cheng *et al*. (11)	59.1±10.2	78	53	14	26	62.9±6.7
	Srivastava *et al*. (12)	62.7±10.5	78	55	16	18	55
	Dhawan *et al*. (13)	63.6±11.5	75	92	28	34	53.9±13.0
	Balkhy *et al*. (14)	66.3±10.4	72	61	7	19	NR
	Jegaden *et al*. (15)	59±12	94	NR	18	NR	59±8
	Srivastava *et al*. (16)	67.4±12.3	51	78	28	41	NR
	Fleck *et al*. (17)	62±5	83	NR	NR	21	62
TECAB on pump	Zaouter *et al*. (19)	64±10	87	74	NR	37	56±12
	Argenziano *et al*. (20)	58±10	81	57	38	22	56.2±10.2
MIDCAB off pump	Yang *et al*. (10)	59.3±9.7	74	52	24	24	63±5.7
	Daniel *et al*. (21)	62.8±12.0	68	90	48	36	55.4±9.3
	Fujita *et al*. (22)	64±10	82	73	36	30	NR
	Halkos *et al*. (23)	59.1	71	NR	NR	NR	49
	Leyvi *et al*. (24)	64.8±12.5	69	NR	39	51	54.2±10.6
	Bayramoglu *et al*. (25)	59.7±9.7	76	50	NR	24	61.8±6.6
	Hemli *et al*. (26)	64.5	65	NR	NR	38	53.4±11.0
	Liu *et al*. (27)	64±11	81	79	NR	46	52±13
	Daniel *et al*. (28)	NR	NR	NR	NR	NR	NR
	Poston *et al*. (29)	66.2±10.1	63	80	56	43	NR
	Srivastava *et al*. (30)	67.2±9.6	66	78	28	46	NR
	Turner *et al*. (31)	65.9	69	NR	26	21	47.8
	Subramanian *et al*. (32)	63.6±9.6	80	NR	NR	40	NR
	Mariani *et al*. (33)	66±9	88	63	8	16	51±8

TECAB, totally endoscopic coronary artery bypass; MIDCAB, minimally invasive direct coronary artery bypass; NR, not reported; HTN, hypertension; MI, myocardial infarction; LVEF, left ventricular ejection fraction.

grafts were performed in selected patients in two off-pump TECAB studies and six off-pump MIDCAB studies. Robotic-assisted LIMA harvest duration ranged from 26 to 60 minutes. The anastomosis time for the TECAB off-pump and TECAB on-pump groups ranged from 9.6–12.6 and 28–60 minutes, respectively. The mean overall operative time for the off-pump TECAB and off-pump MIDCAB groups ranged from 161–326, and 166–444 minutes, respectively. Pooled conversion rates from the intended incision were 7.0% (95% CI, 2.8–16.9%), 8.9% (95% CI, 1.3–42.7%) and 4.4% (95% CI, 2.9–6.6%) in the off-pump TECAB, on-pump TECAB, and robotic MIDCAB groups, respectively. A summary of these intraoperative outcomes is presented in *Table 3*.

Peri-operative outcomes

Off-pump TECAB

The pooled peri-operative mortality following off-pump TECAB was 1.7% (95% CI, 0.9–3.2%). The rates of peri-operative MI, stroke and acute kidney injury (AKI) were 1.1% (95% CI, 0.5–2.6%), 1.1% (95% CI, 0.4–2.7%) and

Table 3 Surgical details of patients who underwent robotic-assisted coronary artery bypass graft surgery

Surgical technique	Study	Grafts					Operative time (mins)			Conversions
		Mean No.	LAD		LCx	RCA	Total	LIMA harvest	Anastomosis	
			N	%						
TECAB off pump	Yang *et al*. (10)	1	100/100	100	0/100	0/100	219±58	NR	NR	NR
	Cheng *et al*. (11)	1	90/90	100	0/90	0/90	161	26	9.6	0/90
	Srivastava *et al*. (12)	1.5	NR	—	NR	NR	255	34	12.6	0/164
	Dhawan *et al*. (13)	1.8	NR	—	NR	NR	326±139	NR	NR	11/106
	Balkhy *et al*. (14)	1.4	120/120	100	28/120	2/120	NR	NR	NR	3/120
	Jegaden *et al*. (15)	NR	59/59	100	0	0	204±42	NR	NR	19/78
	Srivastava *et al*. (16)	1.5	87/93	94	19/93	7/93	220	NR	13	6/108
	Fleck *et al*. (17)	NR	NR	—	NR	NR	298±110	NR	NR	5/14
TECAB on pump	Zaouter *et al*. (19)	1	38/38	100	0/38	0/38	NR	NR	60±37	1/38
	Argenziano *et al*. (20)	1	85/85	100	0/85	0/85	353±89	60±24	28±11	18/98
MIDCAB off pump	Yang *et al*. (10)	1.0	139/140	99	0/140	2/140	264±70	NR	NR	NR
	Daniel *et al*. (21)	NR	NR	—	NR	NR	NR	NR	NR	NR
	Fujita *et al*. (22)	1	33/33	100	0/33	0/33	NR	NR	NR	3/36
	Halkos *et al*. (23)	1	307/307	100	0/307	0/307	NR	NR	NR	16/307
	Leyvi *et al*. (24)	1	150/150	100	0/150	0/150	222±66	NR	NR	1/150
	Bayramoglu *et al*. (25)	NR	NR	—	NR	NR	166±20	42±6	NR	NR
	Hemli *et al*. (26)	1	77/77	100	0/77	0/77	NR	32±10	NR	NR
	Liu *et al*. (27)	2.8	NR	—	NR	NR	NR	NR	NR	NR
	Daniel *et al*. (28)	NR	NR	—	NR	NR	NR	NR	NR	15/271
	Poston *et al*. (29)	1.9	100/100	100	22/100	0/100	348±72	NR	NR	NR
	Srivastava *et al*. (30)	2.4	132/148	89	119/148	89/148	312±12	NR	NR	NR
	Turner *et al*. (31)	2.2	99/155	64	31/155	21/155	284	NR	NR	3/70
	Subramanian *et al*. (32)	2.2	30/30	100	20/30	16/30	444±49	NR	NR	NR
	Mariani *et al*. (33)	1.8	23/24	97	20/24	0/24	NR	NR	NR	NR

TECAB, totally endoscopic coronary artery bypass; MIDCAB, minimally invasive direct coronary artery bypass; NR, not reported; LAD, left anterior descending; LCx, left circumflex; RCA, right coronary artery; LIMA, left internal mammary artery.

3.4% (95% CI, 1.2–9.7%), respectively. Re-operation for bleeding was required in 3.2% (95% CI, 1.6–6.3%) and peri-operative atrial fibrillation was reported in 11.7% (95% CI, 8.0–16.8%). Pooled post-operative ventilation time was 8.7 hours (95% CI, 1.5–15.9), and the pooled length of hospital and intensive care unit (ICU) stay was 5.6 days (95% CI, 3.5–7.7) and 32.0 hours (95% CI, 14.6–49.4), respectively.

Robotic MIDCAB

The pooled peri-operative mortality following robotic MIDCAB was 1.0% (95% CI, 0.6–1.6%). The rates of peri-operative MI, stroke and AKI were 1.2% (95% CI, 0.7–2.1%), 0.7% (95% CI, 0.3–1.5%) and 1.8% (95% CI, 1.1–2.9%), respectively. Re-operation for bleeding was required in 2.7% (95% CI, 1.9–3.8%), peri-operative atrial fibrillation was reported in 12.5% (95% CI, 9.2–16.8%)

Table 4 Mortality rates, ventilation times and length of stay in hospital and ICUs of patients who underwent robotic-assisted coronary artery bypass graft surgery

Technique	Study	30-day mortality (%)	Ventilation time (h)	ICU time (h)	Mean LOS (d)	Mortality beyond 30 days (%)	Follow-up period
TECAB off pump	Yang *et al*. (10)	0/100 (0)	13.9±4.0	40.8±21.1	NR	NR	NR
	Cheng *et al*. (11)	0/90 (0)	6.77	26.3	NR	NR	NR
	Srivastava *et al*. (12)	1/164 (0.6)	NR	NR	NR	3/56 (5.4)	13 months
	Dhawan *et al*. (13)	4/106 (3.8)	NR	NR	NR	NR	NR
	Balkhy *et al*. (14)	1/120 (0.8)	NR	NR	3.3±2.4	1/120 (0.8)	6–12 months
	Jegaden *et al*. (15)	1/59 (1.7)	4.6±2.4	23.0±19.2	5.5±1.6	2/59 (3.4)	3 years
	Srivastava *et al*. (16)	0/93 (0)	NR	NR	NR	NR	NR
	Fleck *et al*. (17)	0/14 (0)	7.6±5.5	31.2	8.4±2.8	NR	NR
TECAB on pump	Zaouter *et al*. (19)	0/38 (0)	NR	21	8	0/14 (0)	4–15 months
	Argenziano *et al*. (20)	0/85 (0)	14±28	35±37	5.1±3.4	0/85 (0)	3 months
MIDCAB off pump	Yang *et al*. (10)	0/140 (0)	15.2±4.5	50.4±50.4	NR	NR	NR
	Daniel *et al*. (21)	1/322 (0.3)	19.0	42.7	4.8	1/100 (1.0)	3.5 years
	Fujita *et al*. (22)	0/33 (0)	NR	NR	NR	NR	NR
	Halkos *et al*. (23)	4/307 (1.3)	2	24	4	NR	NR
	Leyvi *et al*. (24)	0/150 (0)	NR	NR	6	NR	NR
	Bayramoglu *et al*. (25)	0/100 (0)	5.8±3	14.4±2.6	5.5±1.7	4/100 (4.0)	8 years
	Hemli *et al*. (26)	0/110 (0)	NR	NR	4	NR	NR
	Liu *et al*. (27)	3/255 (1.2)	NR	NR	NR	NR	NR
	Daniel *et al*. (28)	4/271 (1.5)	NR	NR	NR	NR	NR
	Poston *et al*. (29)	0/100 (0)	4.8±6.3	21.9±9.3	3.8±1.5	NR	NR
	Srivastava *et al*. (30)	0/148 (0)	NR	NR	3.6±2.9	0/84 (0)	13 months
	Turner *et al*. (31)	0/70 (0)	4.6±1.5	NR	4.5	NR	NR
	Subramanian *et al*. (32)	0/30 (0)	NR	NR	NR	NR	NR
	Mariani *et al*. (33)	0/24 (0)	7 ± 2	13±8	3.4±2.0	NR	NR

TECAB, totally endoscopic coronary artery bypass; MIDCAB, minimally invasive direct coronary artery bypass; NR, not reported; ICU, intensive care unit; LOS, length of stay.

and wound infection occurred in 1.9% (95% CI, 1.2–3.1%). Pooled post-operative ventilation time was 8.7 hours (95% CI, 5.6–11.8), and the pooled length of hospital and ICU stay was 4.7 days (95% CI, 3.7–5.7) and 26.7 hours (95% CI, 19.9–33.4), respectively. A summary of these perioperative outcomes is presented in *Tables 4,5* and *6*. There was insufficient data to statistically summarize clinical outcomes following on-pump TECAB from the limited number of studies.

Anastomotic complications and long-term outcomes

Anastomotic complications were reported using heterogeneous endpoints, such as graft occlusion, graft failure and graft stenosis. Postoperative routine imaging of coronary grafts by angiography or CTCA was performed in 12 out of 25 studies. In the remaining studies, graft complications were detected by investigation of symptomatic patients. The reported rates of graft occlusion ranged from 0–6.7%,

Table 5 A summary of perioperative complications in patients who underwent robotic-assisted coronary artery bypass graft surgery

Technique	Study	MI (%)	Repeat revascularization (%)	AF (%)	Re-operation (%)	AKI (%)	Wound Infection	Stroke (%)
TECAB off pump	Yang *et al*. (10)	0/100 (0)	2/100 (2.0)	NR	1/100 (1)	NR	NR	0/100 (0)
	Cheng *et al*. (11)	0/90 (0)	NR	NR	NR	NR	NR	NR
	Srivastava *et al*. (12)	1/164 (0.6)	NR	13/164 (7.9)	4/164 (2.4)	4/164 (2.4)	NR	NR
	Dhawan *et al*. (13)	NR	NR	17/106 (16)	NR	NR	NR	NR
	Balkhy *et al*. (14)	1/120 (0.8)	NR	NR	2/120 (1.7)	NR	0/120 (0)	1/120 (0.8)
	Jegaden *et al*. (15)	2/59 (3.4)	4/59 (6.8)	NR	5/59 (8.5)	NR	NR	0/59 (0)
	Srivastava *et al*. (16)	0/93 (0)	1/93 (1.1)	12/93 (13.0)	NR	1/93 (1.1)	NR	0/93 (0)
	Fleck *et al*. (17)	NR	NR	1/14 (7.1)	NR	NR	NR	NR
TECAB on pump	Zaouter *et al*. (19)	0/38 (0)	NR	7/33 (21.0)	0/38 (0)	0/38 (0)	0/38 (0)	0/38 (0)
	Argenziano *et al*. (20)	1/85 (1.2)	4/85 (4.7)	1/85 (1.2)	3/85 (3.5)	1/85 (1.2)	5/85 (5.9)	NR
MIDCAB off pump	Yang *et al*. (10)	0/140 (0)	1/140 (0.7)	NR	0/140 (0)	NR	4/140 (2.9)	0/140 (0)
	Daniel *et al*. (21)	NR	NR	NR	9/322 (2.8)	NR	NR	NR
	Fujita *et al*. (22)	0/33 (0)	NR	NR	NR	NR	NR	0/33 (0)
	Halkos *et al*. (23)	5/307 (1.6)	NR	47/307 (15.0)	7/307 (2.3)	6/307 (2.0)	6/307 (2.0)	1/307 (0.3)
	Leyvi *et al*. (24)	NR	NR	19/150 (13.0)	2/150 (1.3)	0/150 (0)	0/150 (0)	2/150 (1.3)
	Bayramoglu *et al*. (25)	0/100	NR	0/100 (0)	NR	0/100 (0)	0/100 (0)	NR
	Hemli *et al*. (26)	NR	NR	NR	3/110 (2.7)	1/110 (0.9)	NR	NR
	Liu *et al*. (27)	NR	NR	NR	NR	NR	NR	NR
	Daniel *et al*. (28)	0/271 (0)	NR	NR	NR	3/271 (1.1)	NR	NR
	Poston *et al*. (29)	1/100 (1.0)	1/100 (1.0)	12/100 (12.0)	1/100 (1.0)	3/100 (3.0)	0/100 (0)	0/100 (0)
	Srivastava *et al*. (30)	0/150 (0)	NR	14/150 (9.3)	5/150 (3.3)	4/150 (2.7)	0/150 (0)	0/150 (0)
	Turner *et al*. (31)	1/70 (1.4)	NR	6/70 (8.6)	2/70 (2.9)	0/70 (0)	2/70 (2.9)	0/70 (0)
	Subramanian *et al*. (32)	NR	NR	NR	2/30 (6.7)	NR	1/30 (3.3)	NR
	Mariani *et al*. (33)	1/24 (4.1)	NR	NR	1/24 (4.2)	NR	NR	NR

TECAB, totally endoscopic coronary artery bypass; MIDCAB, minimally invasive direct coronary artery bypass; NR, not reported; MI, myocardial infarction; AF, atrial fibrillation; AKI, acute kidney injury.

and the rates of graft or anastomotic stenosis ranged from 0.7–13%. Due to the variable timing of follow-up imaging and definitions of anastomotic complications, formal statistical analysis of this endpoint could not be performed. A summary of the reported data on graft complications is presented in *Table 7*. Mortality beyond 30 days was reported at variable time frames ranging from three months to eight years, ranging from 0–5.4%. Due to the lack of standardized time intervals, detailed statistical analysis could not be performed. Reported outcomes for long-term mortality are summarized in *Table 4*.

Discussion

The ultimate goal of robotic CABG is to perform safe and effective coronary anastomoses through a minimally invasive approach to enhance recovery and minimize trauma. To achieve this goal, a number of techniques

Table 6 Summary of postoperative outcomes for off-pump total endoscopic coronary artery bypass grafting (TECAB) and minimally invasive direct coronary bypass grafting (MIDCAB) in all included studies

Perioperative outcome	% incidence (95% confidence interval)
TECAB off-pump	
Mortality	1.7% (0.9–3.2%)
MI	1.1% (0.5–2.6%)
Stroke	1.1% (0.4–2.7%)
Acute kidney injury	3.4% (1.2–9.7%)
Reop bleeding	3.2% (1.6–6.3%)
Atrial fibrillation	11.7% (8.0–16.8%)
Ventilation time (hours)	8.7 (1.5–15.9)
Hospital stay (days)	5.6 (3.5–7.7)
ICU stay (hours)	32.0 (14.6–49.4)
MIDCAB off-pump	
Mortality	1.0% (0.6–1.6%)
MI	1.2% (0.7–2.1%)
Stroke	0.7% (0.3–1.5%)
Acute kidney injury	1.8% (1.1–2.9%)
Reop bleeding	2.7% (1.9–3.8%)
Atrial fibrillation	12.5% (9.2–16.8%)
Wound infect	1.9% (1.2–3.1%)
Ventilation time (hours)	8.7 (5.6–11.8)
Hospital stay (days)	4.7 (3.7–5.7)
ICU stay (hours)	26.7 (19.9–33.4)

ICU, intensive care unit; MI, perioperative myocardial infarct.

and robotic systems have been developed over the past 15 years, culminating in a totally endoscopic approach using the da Vinci operating system, without the need for cardiopulmonary bypass, also known as the off-pump TECAB technique. Although LIMA was commonly grafted onto the LAD as a single TECAB graft, robotic harvesting of bilateral mammary arteries was feasible and all territories of the heart could be grafted robotically (14). From a historical perspective, the AESOP system was initially developed as a voice-activated robot used to hold an endoscope, and approved by FDA for minimally invasive surgery in 1994. This was followed by the Zeus Robotic Surgical System (Computer Motion Inc., Goleta, CA, USA), which consisted of two robotic arms mounted to the patient bed, controlled via a satellite control unit. The Zeus system was discontinued from clinical use in 2003, following the introduction of the da Vinci system, which consisted of three principle components: (I) a surgical console; (II) a computer controlled system; and (III) robotic manipulations. The surgeon was positioned at the console to grasp specially designed instrument handles. The surgeon's motions were then relayed to a computer processor, which digitized the surgeon's hand motions. The digitized information from the computer control system was then relayed in real time to robotic manipulators, which were attached to the operating room table. These manipulators held the endoscopic instrument tips, which were inserted through small ports, performing all aspects of the CABG procedure without sternotomy or thoracotomy (31).

Current limitations to the robotic CABG technique include its cost, heterogeneous clinical outcomes, limited training opportunities and evolving instrumentation for the endoscopic technique. From a technical perspective, one of the greatest challenges to robotic-assisted CABG is the anastomosis of the LIMA-to-LAD graft. To perform this critical step, the distal end of the LIMA is skeletonized prior to anastomosis, and the target coronary artery is identified and positioned. If TECAB is performed off-pump, silastic bands or saddle loops can be placed either side of the anastomotic site for vessel occlusion prior to arteriotomy. Some authors advocated the use of ischemic preconditioning (14) or intra-coronary shunt placement (18,26). The target vessel can be opened using an endoscopic knife and the arteriotomy performed with endoscopic Potts scissors. The distal anastomosis can be performed using robotic endoscopic sutures, U-clips (Medtronic, Minneapolis, MN, USA), or anastomotic devices such as the C-Port Flex A (Cardica, Redwood City, CA, USA). Distal anastomotic patency can be checked intraoperatively via angiography or ultrasonography (11,14), or postoperatively using CTCA (17), Doppler ultrasonography (18) or formal angiography. Overall, it has been acknowledged that robust clinical outcomes, as well as improved instrumentation at affordable costs will be critical to the future development of the TECAB technique.

The present systematic review found that the majority of studies on robotic-assisted CABG procedures involved patients who underwent off-pump TECAB or robotic-assisted MIDCAB techniques. This was not an unexpected finding, as the use of cardiopulmonary bypass was

Table 7 Graft complications of patients who underwent robotic-assisted coronary artery bypass graft surgery

Technique	Study	Routine graft assessment	Assessment technique	Time of assessment	Graft occlusion (%)	Graft failure	Anastomotic or graft stenosis (%)
TECAB off pump	Yang *et al*. (10)	Yes	Mixed	5 years	1/67 (1.5)	NR	3/23 (13.0)
	Cheng *et al*. (11)	Yes	Angiogram	Before discharge	0/90	NR	2/90 (2.2)
	Srivastava *et al*. (12)	Yes	Mixed	Before discharge	1/214 (0.5)	4/164 (2.4)	3/164 (1.8)
	Dhawan *et al*. (13)	No	NR	NR	3/106 (2.8)	NR	7/106 (6.6)
	Balkhy *et al*. (14)	Yes	Angiogram	4 months	5/85 (5.9)	NR	NR
	Jegaden *et al*. (15)	Yes	CTCA	3 years	3/53 (5.7)	NR	3/53 (5.6)
	Srivastava *et al*. (16)	Yes	Mixed	26 days	0/93 (0)	NR	NR
	Fleck *et al*. (17)	Yes	CTCA	Before discharge	0/14 (0)	NR	NR
TECAB on pump	Zaouter *et al*. (19)	No	NR	NR	NR	2/38 (5.2)	NR
	Argenziano *et al*. (20)	Yes	Angiogram	3 months	1/85 (1.2)	NR	NR
MIDCAB off pump	Yang *et al*. (10)	Yes	Mixed	5 years	1/67 (1.5)	NR	3/23 (13.0)
	Daniel *et al*. (21)	No	NR	NR	NR	NR	NR
	Fujita *et al*. (22)	Yes	CTCA	Before discharge	0/33 (0)	NR	NR
	Halkos *et al*. (23)	No	NR	NR	5/199 (2.5)	10/307 (3.3)	3/199 (0.7)
	Leyvi *et al*. (24)	No	NR	NR	NR	NR	NR
	Bayramoglu *et al*. (25)	Yes	Mixed	8 years	6/106 (5.7)	NR	NR
	Hemli *et al*. (26)	No	NR	NR	NR	NR	NR
	Liu *et al*. (27)	No	NR	NR	NR	NR	NR
	Daniel *et al*. (28)	NR	NR	NR	NR	NR	NR
	Poston *et al*. (29)	Yes	CTCA	12 months	1/100 (1.0)	NR	NR
	Srivastava *et al*. (30)	No	NR	NR	2/148 (1.4)	NR	NR
	Turner *et al*. (31)	No	NR	NR	2/70 (2.9)	NR	NR
	Subramanian *et al*. (32)	No	NR	NR	2/30 (6.7)	NR	NR
	Mariani *et al*. (33)	No	NR	NR	NR	NR	NR

TECAB, totally endoscopic coronary artery bypass; MIDCAB, minimally invasive direct coronary artery bypass; NR, not reported; CTCA, computed tomography coronary angiogram.

acknowledged as a 'stepping stone' to off-pump TECAB for surgeons who were overcoming their technical learning curves (20). Although cardiopulmonary bypass and cardioplegia allowed the surgeon to operate on an arrested heart, the addition of peripheral cannulation and aortic clamping prolonged the operative duration, and added complications such as groin wound infections and vascular injuries (20). The patients included in the selected studies in the present systematic review were relatively young, with a mean age in the 60s, and well-preserved preoperative left ventricular function, with a mean ejection fraction of >55% in the majority of studies. In addition, the numbers of anastomoses were relatively few, especially for the TECAB groups, which averaged less than two grafts in all of the studies, and almost exclusively for the LIMA-to-LAD graft. Keeping these considerations in mind, results of the present systematic review demonstrated relatively safe perioperative outcomes for both the off-pump TECAB and robotic MIDCAB groups, with a pooled perioperative mortality rate of 1.7% and 1.0%, respectively. Dhawan and colleagues reported a relatively high perioperative mortality rate of 3.8% from a cohort of 106 patients, with four deaths within the perioperative period related to cardiogenic shock, fibrillatory arrest or bleeding (13). Other perioperative outcomes, such as MI, stroke, AKI, re-operation for bleeding and atrial fibrillation were comparable to contemporary data for conventional CABG procedures (54,55). Other key findings of the study included anastomotic complication rates that ranged from 0.7–13%. However, routine follow-up varied in relation to angiographic assessment technique, timing, and definition of endpoints. Long-term survival was also difficult to assess due to limited and non-systematic follow-up of patient cohorts, but the available data reported favorable outcomes, including one report of 4% mortality at 8-year follow-up.

Some of the unexpected results can be rationalized with detailed examination of the surgical technique performed. For example, Zaouter *et al*. reported a relatively long anastomosis time of 60 minutes (19). However, this duration was measured from the time of LIMA occlusion, and included the period of time spent on target vessel identification and preparation prior to anastomosis. Similarly, although Srivastava, Poston and Subramanian reported mean total operative times of 311, 348 and 444 minutes, respectively, they also averaged 1.9–2.2 grafts, accounting for the increased operative time spent on conduit harvesting and performing the additional anastomoses (29,30,32). In addition, studies of on-pump TECAB, such as the multi-institutional study by Argenziano and colleagues, reported longer operative times due to the need for peripheral cannulation and use of a cardiopulmonary circuit (20). Finally, perioperative outcomes such as ventilation time, ICU stay, and total hospitalization time were dependent on clinical pathways specific to each institution, and prolonged times may have been multi-factorial (10).

A number of important limitations to the present systematic review should be acknowledged, and reported outcomes should be interpreted with caution. Firstly, only non-randomized, observational studies were identified, and robust comparisons with conventional CABG through the sternotomy approach were not possible using directly comparative data. Secondly, it should be noted that the patient cohort included in the present systematic review were a highly selected subgroup, with relatively favorable baseline patient characteristics, and should not be generalized to all patients with coronary artery disease, especially those who present with acute coronary syndrome. Thirdly, surgical techniques evolved over time, partly due to the learning curve of individual surgeons and institutions, and also partly due to the evolution of instrumentation available in clinical practice. Variations in surgical techniques and experience may have accounted for some of the differences between the selected observational studies.

Conclusions

Overall, the present systematic review examined the current evidence for robotic-assisted CABG procedures, which were mostly focused on the off-pump TECAB and off-pump MIDCAB techniques. Statistical analysis demonstrated relatively safe outcomes using perioperative mortality as the primary endpoint. However, there remains a paucity of robust clinical data related to anastomotic complications, and future studies should follow standardized, routine angiographic follow-up at predefined time intervals to demonstrate technical efficacy. Results of the present systematic review should be considered as a useful benchmark for future studies on robotic CABG, until further data is reported from randomized studies.

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Footnote

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