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MASTER THESIS

THE ROLE OF ROBOTICS IN CARDIAC SURGERY

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Περίληψη

Εισαγωγή/Σκοπός: Η χρήση της τεχνολογίας και των εφαρμογών της ρομποτικής χειρουργικής στην καρδιοχειρουργική έχουν καταστήσει εφικτή την πρόσβαση στην θωρακική κοιλότητα με την αποφυγή στερνοτομής. Δεδομένης της πολλά υποσχόμενης υπάρχουσας βιβλιογραφίας, πραγματοποιήσαμε μία συστηματική ανασκόπηση της βιβλιογραφίας σχετικά με την αποτελεσματικότητα, τις εφαρμογές και την θνητότητα που σχετίζονται με τη ρομποτική καρδιοχειρουργική.

Μεθοδολογία: Πραγματοποιήθηκε ενδελεχής έρευνα των ακολούθων μηχανών αναζήτησης: Pubmed και Cochrane με την χρήση των εξής ορολογιών: «ρομποτική», «καρδιοχειρουργική» και «χειρουργείο καρδιάς». Μόνο μελέτες ρομποτικής καρδιοχειρουργικής με τουλάχιστον 10 ασθενείς και που ανέφεραν αποτελέσματα για περιεγχειρητική θνητότητα συμπεριελήφθησαν στην εν λόγω ανάλυση.

Αποτελέσματα: Συνολικά 28 μελέτες συμπεριελήφθησαν και παρουσιάζουν δεδομένα για 5.993 ασθενείς με μέση ηλικία τα 59,8 έτη. Σχεδόν ένας στου δύο ασθενείς (49,2%) υπεβλήθη σε ρομποτική αορτοστεφανιαία παράκαμψη, ενώ σχεδόν το άλλο μισό των ασθενών (49,9%) υπεβλήθη σε ρομποτική αντικατάσταση μιτροειδούς βαλβίδας. Η μέση θνητότητα κατά τις πρώτες 30 μέρες μετεγχειρητικά ήταν 0,7% και κυμαινόταν από 0% μέχρι 0,8% ανεξαρτήτως τύπου χειρουργείου, ενώ η θνητότητα και την περίοδο παρακολούθησης των ασθενών μετά το πέρας της νοσηλείας τους ήταν κατά μέσο όρο 0,8% και κυμαινόταν από 0% έως 1% για μέσο χρόνο παρακολούθησης 40.1 μήνες.

Συμπεράσματα: Τα ευρήματά μας δείχνουν ότι οι εφαρμογές της ρομποτικής καρδιοχειρουργικής έχει προσφέρει μία ασφαλή και αποτελεσματική εναλλακτική στις παραδοσιακές τεχνικές χειρουργικής. Ωστόσο, χρειάζονται περεταίρω μελέτες για να διαφωτιστούν όλες οι πτυχές της.

Λέξεις κλειδιά: ρομποτική καρδιοχειρουργική, ρομποτικά υποβοηθούμενη, ενδοσκοπική

Abstract

Background: The application of robotic technologies in cardiac surgery has provided the possibility for minimally invasive access inside the thorax and avoidance of a median sternotomy. Given that current evidence seems promising, we sought to systematically review the existing literature regarding the efficacy, feasibility and mortality rate associated with robotic cardiac surgery.

Methods: The PubMed and Cochrane bibliographical databases were thoroughly searched for the following MeSH terms: "robotic", "cardiac surgery" and “heart surgery”. Original studies on robotic cardiac surgery in more than ten cases and reporting on the associated peri- or post-operative mortality were deemed eligible.

Results: Twenty-eight studies were included and provided data for 5,993 patients with a mean age of 59.8 years. Approximately one out of two patients (49.2%) underwent robotic CABG, while the other half (49.9%) underwent robotic MVR. Robotic atrial septal defect repair and atrial tumor resection was performed in a small proportion (0.9%) of the patients. Mean 30-day mortality was 0.7% ranging from 0 to 0.8% among the different types of surgery, while late mortality was 0.8% ranging from 0 to 1% with a mean follow-up period of 40.1 months.

Conclusions: Our findings demonstrate that the application of robotics in cardiac surgery has provided a safe and efficacious alternative to the traditional techniques. However, more trials are necessary to elucidate all of its aspects.

Keywords: robotic cardiac surgery; robotically-assisted; endoscopic

Ευχαριστίες

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Δεν θα μπορούσα να παραλείψω τη **κα. Μαρία Παναγιωτακοπούλου**, Γραμματέα του μεταπτυχιακού προγράμματος χωρίς τη βοήθεια, στήριξη και άμεση ανταπόκριση της δεν θα ήταν δυνατή η ολοκλήρωση της εν λόγω πτυχιακής εργασίας. Η κα. Παναγιωτακοπούλου φάνηκε αντάξια των περιστάσεων και παρά τις απρόσμενες δυσκολίες που προέκυψαν λόγω του Covid-19 κατάφερε με μεγάλη επιτυχία να φέρει εις πέρας όλες τις απαραίτητες διεργασίες για την ομαλή λειτουργία του προγράμματος.

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Introduction

Conventional open cardiac surgery carries an increased operation risk and requires a large incision, long hospitalization and recovery time[1]. Minimally invasive approaches applied in cardiac surgery have been shown to significantly merit patients in terms of minimized surgical trauma, reduced need for analgesia and faster recovery[1]. Since its introduction in the late 90's, robotic cardiac surgery has gained increased acceptance in a number of cardiac surgical procedures including coronary artery bypass grafting (CABG), mitral valve repair/replacement (MVR), cardiac tumor resection and atrial septal defect (ASD) closure[2].

Several studies have aimed to evaluate the safety and efficacy of robotic cardiac surgery. A recently published meta-analysis of 16 studies, which compared totally endoscopic coronary artery bypass (TECAB) and robotically assisted coronary artery bypass (RACAB) with conventional CABG showed that both minimally invasive techniques are safe and feasible[3]. Another systematic review of robotic mitral valve surgery by Seco et al[4], concluded that the application of robotics is a viable option for every type of mitral valve surgery and that it is associated with acceptable mortality rates (0-3%). Furthermore, a review of the robotic cardiac operations performed in Europe suggested a long-year experience with robotic CABG and a much shorter with robotic MVR, but with low peri-operative complications[2].

Cumulative evidence on the mortality rates associated with robotic cardiac surgery is still inconclusive. To that end, the objective of our study was to systematically review the existing literature for all types of robotic cardiac surgery and establish a comprehensive overview of the post-operative mortality associated with these novel surgical approaches.

Methods

Search strategy and Eligibility of Studies

The present systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) guidelines and in line with the protocol agreed by all authors. PubMed and Cochrane bibliographic databases were thoroughly searched from January 1986 to February 2018 (last search: March 4th, 2018). Two investigators (I.D and E.S.) worked independently and executed the search using the following MeSH terms: "robotic", "cardiac surgery" and "heart surgery". A manual search of additional articles was conducted using references from relevant articles and review papers. Any discrepancies were resolved by consensus agreement by a third reviewer (M.S.).

Original clinical studies written in English on the applications of robotic surgery in cardiac surgery in more than 10 cases and reporting on the associated peri- or post-operative mortality were included in the present study. Excluded studies met at least one of the following criteria: 1) papers published in a language other than English, 2) studies not showing mortality data explicitly for patients undergone robotic cardiac surgery 3) studies which included patients that solely underwent robotic ablation or resynchronization, 4) case-reports, 5) experimental studies in animals, 6) studies in non-adults, 7) studies reporting on data from large-scale databases, 8) reviews and meta-analyses, 9) editorials and letters to the editor and 10) papers with irrelevant to our study data, such as epidemiological data, anesthesia techniques, etc.

Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors.

Data Extraction

Data were extracted regarding type of operation, robotic technique and surgical system used, country of origin, Newcastle Ottawa Scale (NOS), study timeframe, number of patients who underwent cardiac robotic surgery, patient demographics (gender, age, body mass index (BMI)), patient co-morbidities (such as known hypertension, diabetes mellitus, dyslipidemia) presence of angina, smoking status, history of myocardial infarction (MI), cerebrovascular disease, peripheral vascular disease, chronic obstructive pulmonary disease (COPD), percutaneous primary coronary intervention (PCI), euroSCORE, presence of single or multi-vessel disease and pre-operative ejection fraction (EF). Peri-operative data such as urgency for operation, total operative time, ventilation time, cardiopulmonary bypass (CPB) time, cross-clamp (XC) time, on-pump time, intensive care unit (ICU) stay and length of stay (LoS) were also extracted. Post-operative complications (conversion, myocardial infarction (MI), cerebrovascular accident (CVA), atrial fibrillation (AF), bleeding, pneumonia, renal failure, infection, anastomotic stenosis, re-operation, late re-intervention and major adverse cardiac and cerebrovascular events (MACCE) were also noted down. Short-term mortality was defined as the mortality rate in the first 30 days after the operation, whereas long-term mortality referred to a period over 30 days after surgery.

Statistical Analysis

The extracted data were incorporated into tables and analyzed regarding the type of operation, namely CABG (TECAB and non-TECAB), MVR and other (ASD repair and atrial myxoma resection). A cumulative analysis of the extracted data was also performed and a descriptive approach was adopted in all parameters. No further statistical analysis was attempted.

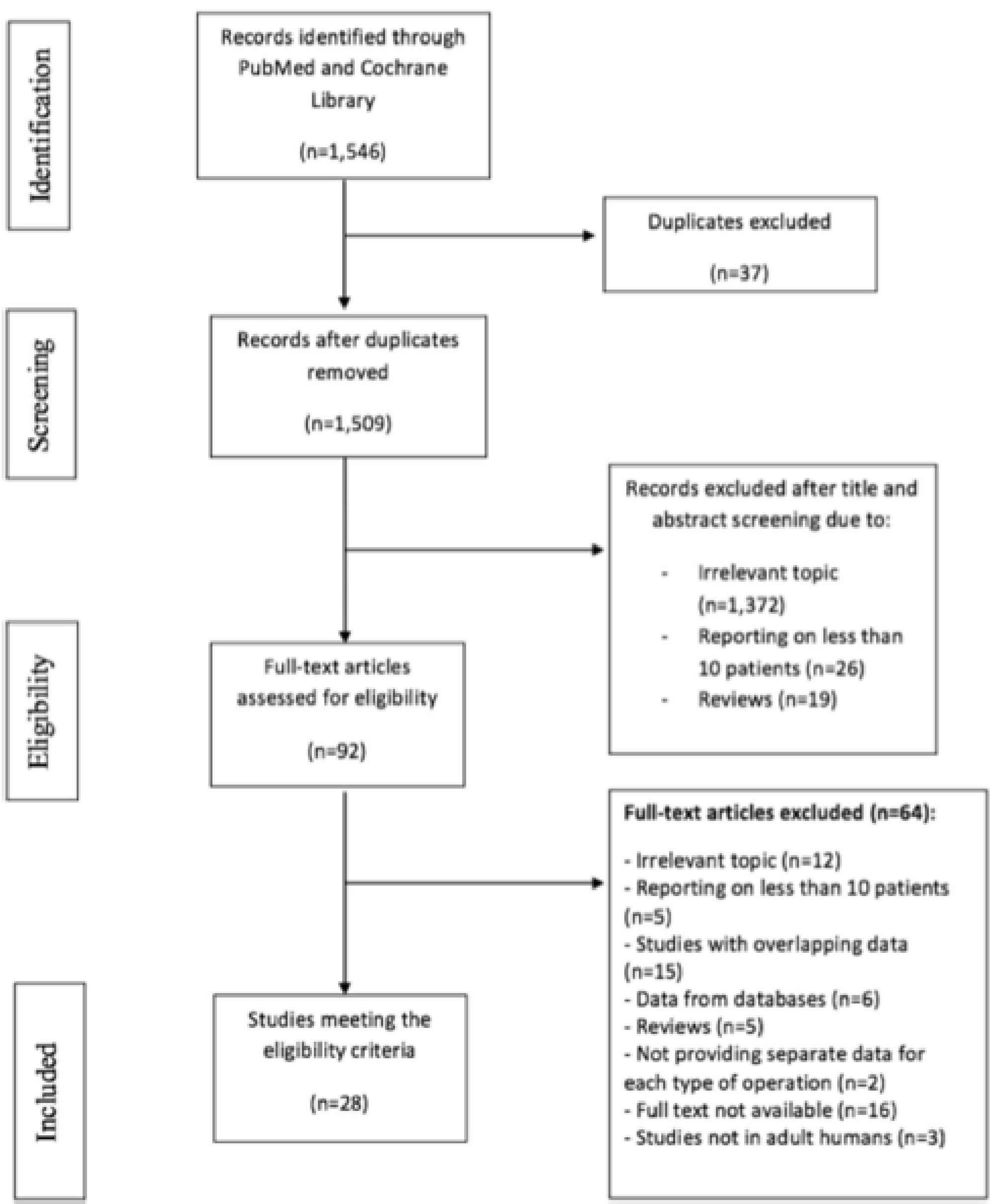
Results

Article selection algorithm and study characteristics

The literature search of both databases generated 1,546 articles. The trial flow diagram, according to PRISMA guidelines, is presented in Figure 1.

Figure 1**.** Flowchart of the included studies according to PRISMA Statement.

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses



Study characteristics and patient demographics are summarized in Table 1. In total, 28 studies were deemed eligible and provided data for 5,993 patients who had undergone robotic cardiac surgery between 1996 and 2016. References of the studies are summarized in Supplemental Table 1. Ten studies[5–14] were conducted in Europe, six in the US[15–20], three in China[21–23], two in Canada[24, 25] and the rest in four other countries. DaVinci robot (included S and Si versions) was utilized in all cases except for the study of Giambruno et al[25], in which Zeus and Automated Endoscopic System for Optical Positioning (AESOP) robotic surgical systems were also used. The data extracted are presented with respect to the type of surgery performed. Major comorbidities per type of surgery are summarized in Table 2, peri-operative data in Table 3 and mortality data in Table 4.

CABG

Major comorbidities

Cumulatively, 2,947 patients underwent robotic CABG, of which, 1,482 underwent TECAB and 1,465 underwent non-TECAB. The majority of the patients were male (75.2%). Overall mean age was 59.5 years and BMI was 26.9 k/m_2. Angina was present in 65.9% (621/943), dyslipidemia in 64.8% (902/1,391), hypertension in 59.6% (1,075/1,803) and diabetes in 40.7% (981/2,408) and of the patients. History of MI was present in 25.4% (359/1,413), while 26% (486/1,869) of the patients had undergone PCI. Mean euroSCORE was 2.3, while data on Society of Thoracic Surgeons (STS) score, New York Heart Association (NYHA) score, Canadian Cardiovascular Society (CCS) grading of angina and left ventricular grade were insufficient. 75.7% (1,039/1,373) of the patients underwent CABG for single vessel disease and their EF was 61.3%.

Peri-operative data and clinical outcomes

Approximately, one out of two (58.3%, 508/872) operations was on-pump with a total operating time of 249.9 minutes, CPB time of 87.3 minutes, XC time of 61.3 minutes and ventilation time of 9.9 hours. Mean ICU stay and LoS were 28.5 hours and 5.2 days, respectively. Conversion to open surgery was the most common complication (7%, 173/2,442) followed by atrial fibrillation (5.5%, 134/2,437) and bleeding (2.3%, 42/1,826), while the rate of MI, CVA, pneumonia, renal failure, infection, anastomotic stricture and re-operation was below 2%. 30-day mortality of the whole population was 0.6%, while late-mortality (data drawn from 2,041 patients) was 2.2%. In the subpopulation of the patients undergone TECAB, 30-day mortality was 0.9% (14/1,504) and late mortality was 2.4% (33/1,403). As far as the non-TECAB patients are concerned, 30-day and late mortality was 0.3% (3/1,065) and 3.2% (12/370), respectively. Need for late re-intervention was prevalent in 1% (26/2,410) of the patients, while the rate of MACCE was 12.2% (181/1,484), in a mean follow-up period of 36.6 months.

MVR

Major comorbidities

In total, 2,993 patients underwent robotic MVR. Of them, 65.6% (1,964/2,993) were male, aged averagely 56.8 years and with a mean BMI of 25.8 kg/m$_2$. Most common comorbidities were hypertension (47.4%, 1380/2,911) and dyslipidemia (22.7%, 46/203), while one out of three patients was a smoker (30.8%, 21/68). NYHA score was higher than II in 33.9% (892/2,631) of the patients and the mean euroSCORE was 2.7. Mean pre-operative EF was 60.7%. Data retrieved from 1,636 patients showed that 77.8% of them had severe (grade 4) mitral regurgitation.

Peri-operative data and clinical outcomes

Total operative, CPB, XC and ventilation time was 256.9 minutes, 133.3 minutes, 90.5 minutes and 32.1 hours, respectively. Average ICU stay was 29.8 hours, while mean LoS was 6.5 days. Atrial fibrillation was the most common post-operative complication (12.5%, 373/2,984), followed by conversion to open surgery (4.7%, 58/1,234) and bleeding (1.7%, 50/2,941). All other complications had a rate lower than 1%. 76 out of 2,923 (2.6%) patients required re-operation, while late re-intervention was necessary in 3.2% (62/1,938) of the cases. 30-day and late mortality were 0.8% (13/2,993) and 0.4% (6/1,659), respectively, while the incidence of MACCE during a follow-up period of 43.5 months, was 9.4% (36/383).

Atrial myxoma resection and atrial septal defect repair

Nineteen patients underwent robotic atrial tumor resection and 34 underwent robotic ASD repair. Cumulatively, 17.6% were male and the mean age was 40.8 years. All three studies reported on operative data exhibiting an average CPB time of 120.5 minutes and XC time of 48.5 minutes. ICU stay was 23hours and LoS was 8 days. There was no conversion to open surgery and no post-operative complication. No death was noted intra-operatively or within the first 30 days post-surgery in any of the studies, while only study[23] with 100% survival rate reported on late mortality.

Comment

Cardiac surgery represents a field of surgery with technically demanding surgical procedures performed on high risk patients. The need for minimizing the burden of the operation per se on the patient is imperative. The application of robotics may be promising in achieving enhanced results alongside with improved anesthetic monitoring and utilization of novel technologies[5]. Since the introduction of minimally invasive surgery to open heart procedures in 1995[26], the use of robotic systems has gained acceptance from the surgical society[2]. According to the available data, robotic cardiac surgeries are most commonly performed in the case of CABG, MVR and in a much lower frequency for the resection of LA tumors and the repair of ASD, while cumulatively presenting both 30-day and late mortality rate lower than 1% with a mean follow-up period of 40.1 months.

A study by Yanagawa et al[1], which reported on data obtained from the Nationalwide Impatient Sample (NIS) database, showed significantly reduced LoS, complications and mortality (1% in the case of robotically assisted cardiac surgery) in 5,199 patients who underwent robotically assisted cardiac surgery compared with 10,331 propensity-matched patients who underwent nonrobotic cardiac surgery. In another study by Deeba et al[27], a European single-center experience in robotic surgery exhibited zero mortality in a registry of 102 cases.

CABG

Ever since the first TECAB performed by Loulmet et al[28] using the first da Vinci® robotic system in 1998, the use of minimally invasive techniques has been widely spread as proposed by Whellan et al[29]. In this study of the Society of Thoracic Surgeons Adult Cardiac Surgery Database (STS-ACSD) from 2006 to 2012, the authors have observed an increase in the volume of robotically assisted CABG while no difference in peri-operative mortality was noted when compared with non-robotic CABG[29]. Additionally, a meta-analysis of 16 studies by Wang et al[3], concluded that the utilization of robotics in CABG does not lead to increase in mortality, MACCE or need for re-intervention. Our results exhibit a 30-day mortality rate of 0.3% and 0.9% for non-TECAB and TECAB, respectively. However, as far as late mortality is concerned, the rate was 3.2% and 2.4%

for non-TECAB and TECAB, respectively. It may be assumed that the observed difference in the early mortality between the two techniques, albeit subtle, may be owed to the more space provided for surgical maneuvers in the case of non-TECAB technique. However, it is important to highlight that this difference was diminished long-term, supporting the fact that both robotic techniques are feasible and efficacious. Only two studies[5, 8] reported 30-day mortality higher than 2%. In the first study, the participants were octogenarians with a mean age of 82.9 years, a fact that can merely justify the increased observed mortality[8]. Moreover, this was the study with the highest late mortality[8]. The authors of the second study reported a high conversion rate (28%) in their patient series, which may reflect their high risk profile and the subsequent increased risk for mortality[5]. As far as MACCE are concerned, the two studies that reported the highest incidence were also the two with the longest follow-up period (5 years)[30, 31].

Apart from decreased mortality rates, application of robotic systems in CABG provides certain benefits. Thanks to its less invasive nature, robotic CABG is associated with a low rate of infection (0.3%) which is even more promising taken into consideration the fact that the mean BMI in all studies was higher than 25 kg/m^2 and that 40.7% of the included patients had diabetes, since these two parameters are known to be risk factors for wound infection post-operatively in traditional CABG[32]. The majority of the patients had single vessel disease, while only 24.3% of them had multiple vessel disease. In the study of Wiedeman et al, 33.2% of the patients had multiple vessel disease, however the early mortality was as low as 1%[31]. Study timeframe was similar among studies and it ranged from 1998 to 2016, as such, differentiations in mortality in terms of the “age” of the studies were not detectable.

At this point it should also be mentioned that the patients had a low risk profile since both their EF and euroSCORE were not deteriorated. When comparing intraoperative data between TECAB and non-TECAB, an increased operating, ventilation and XC time as well as rate of conversion to open surgery is noted in the case of TECAB, most probably due to the more challenging nature of this procedure. Yet, ICU stay and LoS did not seem to differ between the two surgical approaches, indicating that these intraoperative deviations did not alter the outcome.

MVR

Two decades after the first reported robotically-assisted MVR[26, 33], a number of studies reporting on data of single-center experiences and national databases have established the efficacy and feasibility of this procedure[12, 34, 35]. Specifically, our results manifest that 30-day and late mortality were 0.8% and 0.4%, respectively. Only one of the eligible studies recruited patients before 2000, however the reported mortality was zero[13]. Two studies included more than 1,000 patients and both exhibited a 30-day mortality rate lower that 1%, while only one of them presented data for late long-term mortality which was zero in a follow-up period of 38.3 months[16, 17]. Similar results were yielded by a systematic review of 16 studies including more than 50 patients undergoing robotic cardiac surgery, which showed that early mortality ranged between 0-3% while most of the included case series reported a mortality rate lower than 1%[4]. The introduction of da Vinci Si did not seem to ameliorate the surgical outcomes in terms of morbidity and mortality compared with the previous version of da Vinci, suggesting that latter has still a place in robotic surgical procedures for MVR. All studies that presented data for MACCE showed zero incidence[12, 19, 22] except for the study of Murphy et al[17], in which a rate of 0.9% was noted. However, there are two main differentiations in this study compared with the others and these are the utilization of lateral endoscopic approach with robotics (LEAR) technique and the fact that the majority of the patients had III-IV NYHA score, while the reverse was noted in the rest of the studies. Moreover, it should be also mentioned that both CPB and XC time seemed to be much lower in this study[17].

Mean conversion to open surgery rate was less than 5% -even lower than that of robotic CABG- while the most common complication was AF. Incidence of post-operative AF was 12.5%, which is comparable with that of open surgery[36, 37], since the association of valve pathology and risk for AF is well-established[38]. Need for re-operation was present in 2.6% and bleeding in 1.7% of the cases. All other complications had a rate lower than 1%. Given that four out of five patients (77.8%) had severe MR, the cumulative survival was much greater than that observed in the literature in patients with severe ischemic MR undergoing open MV repair or replacement[39]. Peri-operative data such as CPB and XC time as well as ICU stay and LoS suggest the feasibility of this robotic procedure and the satisfying recovery of the patients. It should be mentioned though, that despite the increased severity of MR, two out of three (66.1%) patients had a I-II NYHA score, while the mean euroSCORE was relatively low (2.7, yet calculated only from two studies).

Other robotic procedures

Available data on robotic cardiac procedures, other than CABG and MVR, are limited and they come from case-series. In our study, we present data from robotic atrial myxoma resection and ASD repair which advocate zero early mortality and post-operative complications. Data on late mortality and patients' comorbidities were not available in any of the studies. A retrospective analysis of the STS database conducted by Moss et al[40] concluded that the utilization of robotics is feasible for LA cardiac tumor resection and it is accompanied by lower blood loss and shorter ventilation time, ICU stay and LoS compared with non-robotic approach. We included one study[23] of LA myxoma robotic resection in our analysis, which exhibited similar ICU stay and LoS with those of the non-robotic arm of the study by Moss et al[40]. Yet, in this study[23], 30-day mortality and surgical complications (including the need for conversion to open surgery) were zero.
The two other eligible studies referred to robotic ASD repair[14, 20]. Both studies reported on totally endoscopic robotic technique, however CPB and XC time was much shorter in the study of Argenziano et al[20]. Yet, it should be taken into account that the aim of the study by Bonaros et al[14] was to evaluate the learning curve of the technique and its association with peri-operative outcomes. Thus said, the CPB and XC time noted towards the plateau of the learning curve are similar to those reported by Argenziano et al[14, 20]. Both studies had similar ICU stay and LoS.

There are certain intrinsic limitations of our study that need to be considered prior to drawing conclusions. The presented data have been retrieved from a relatively large number of studies but no data from randomized control trials (RCTs) are available. In addition, the surgeons' fellowship training and the learning curve for robotic cardiac surgery was not separately evaluated in our analysis. Moreover, data concerning the general cost for application of robotic technology in cardiac surgery was not analyzed.

Although it is beyond the scope of this systematic review, it should be mentioned that the aforementioned cost derives from the price of the robotic system, the cost for its maintenance and its consumables parts and the cost for the training of the surgeons[1]. On the other hand, the optimal results offered by this method lead to decreased mortality and morbidity, a fact that should be also taken into consideration in terms of cost-effectiveness. The initial high cost for obtaining a robotic system in combination with the need for expertise in this technique are the two main reasons why the data shown mainly shrine from large centers specialized in this surgical technology.

The application of robotics in cardiac surgery is associated with low mortality and complication rates regardless of the type of the surgery, which are comparable or even lower than those of open surgery. There seems to be fertile ground for the utilization of robotic technology in the field of cardiac surgery (CABG, MVR, tumor resection and ASD repair) since it can offer the well-documented advantages of minimally invasive surgery with no extra "health cost" for the patient. However, further multicenter RCTs are needed to indisputably prove its efficacy and feasibility.

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Conflict of interest
IPD, ES, NM, DS, DP, MS, DIT, DM, DCI, AT, DD and NIN declare that they have no conflict of interest.

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Appendix A

Author	NOS Stars	Study Origin	Study Period	Operation, n(%)		Method Used	Robotic surgical system used	No of Patients, n	Gender, n	
				Primary	Secondary				Male	Female
Tarola	6	Canada	12/2006-08/2015	CABG	-	MINICAB	da Vinci	90	66	24
Yang	9	China	2007-2014	CABG	-	TECAB	da Vinci	100	84	16
						MINICAB	da Vinci	140	103	37
Wiedeman	9	Austria/USA	2001-2011	CABG	-	TECAB	da Vinci	500	364	136
de Canniere	7	Belgium/Germany	09/1998-11/2002	CABG	-	TECAB	da Vinci	228	-	-
Dogan	6	Germany	06/1999-02/2001	CABG	-	TECAB	da Vinci	45	32	13
Kappert	6	Germany	05/1999-03/2000	CABG	-	MIDCAB	da Vinci	60	42	18
						TECAB	da Vinci	10	9	1
						REDCAB	da Vinci	25	19	6
Giambruno	7	Canada	02/1998-02/2016	CABG	PCI (151/605)	RADCAB	AESOP, Zeus, da Vinci	605	455	150
Kofler	7	Austria/United Arab Emirates		CABG	-	TECAB	da Vinci	280	217	63
Roubelakis	8	Belgium	07/2002-09/20015	CABG	PCI (11/44)	REMIDCAB	da Vinci Si	44	31	13
Hemli	7	USA	01/2010-01/2011	CABG	-	MIDCAB (90/110), TEACB (20/110)	da Vinci	110	75	35
Bonatti	9	Austria/USA	06/2001-06/2011	CABG	PCI (226/226)	TECAB	da Vinci	226	173	53
Jegaden	8	France	01/1998-12/2008	CABG	-	PACAB	da Vinci	48	-	-
						MIDCAB	da Vinci	53	-	-
						TECAB	da Vinci	59	-	-
Sagbas	6	Turkey		CABG	-	SVST/MVST (Mini-thoracotomy)	da Vinci	56	-	-

Mishra	7	India	12/2002-09/2006	CABG	-	TECAB (14/268), MIDCAB (193/268), THORACAB (61/268)	da Vinci	268	213	55
						Sub-total		**2947**	**1883**	**620**
						non TECAB		**1465/2947**	**716/965**	**248/965**
						TECAB		**1482/2947**	**879/1161**	**282/1161**
Kesavuori	9	Finland	05/2011-12/2015	Roboticly asisted MVR	-	-	daVinci Si	142	115	27
Gillinov	7	USA	01/2006-11/2013	Roboticly asisted MVR	-	-	daVinci Si	1000	770	230
Navarra	7	Belgium	02/2012-06/2016	Roboticly asisted MVR	-	-	daVinci Si	134	108	126
Kim	7	Korea	08/2007-12/2015	Robotic MVR	-	-	da Vinci	310	201	109
Murphy	7	USA	01/2006-12/2013	Robotic MVR	-	LEAR	da Vinci S	1257	675	582
Poffo	6	Brazil	03/2010-12/2015	Robotic MVR	Annuloplasty (14/20), PFO Closure (4/20)	-	da Vinci	20	16	4
Folliguet	8	France	02/2004-09/2005	Robotic MVR	-	-	da Vinci	25	16	9
Gao	6	China	01/2007-03/2011	Roboticly asisted MVR	-	-	da Vinci	22	9	13
Bhamidipati	6	USA	08/2004-04/2008	Roboticly asisted MVR	-	-	da Vinci	43	29	14
Tatooles	6	USA	10/2001-10/2002	Roboticly asisted MVR	-	-	da Vinci	25	18	7

Autschbach	6	Germany	06/1996-12/1999	Roboticly asisted MVR	-	-	da Vinci	15	7	8
						Sub-total		**2993**	**1964**	**1129**
Gao	6	China	01/2007-06/2009	Atrial myxoma resection	-	-	da Vinci S	19	-	-
Boanros	6	Austria	03/2003-12/2005	TEASD-R	-	-	daVinci	17	3	14
Argenziano	6	USA	-	ASD/PFO	-	-	daVinci	17	-	-
						Sub-total		**83**	**3**	**14**
						Total		5993	3850	1763

Table 1. Study characteristics and patient demographics of the included studies according to type of surgery (CABG, MVR, other) as well as cumulative presentation of the data.

**NOS: Newcastle-Ottawa Scale; CABG: Coronary artery bypass; MINICAB: Mini-thoracotomy CABG; TECAB: Total endoscopic CABG; MIDCAB: Minimally invasive CABG; REDCAB: Robotically enhanced CABG; PCI: Percutaneous coronary intervention; RADCAB: Robotically assisted CABG; AESOP: Automated Endoscopic System for Optical Positioning; REMIDCAB: Robotic-enhanced minimally invasive direct; PACAB: Port-Access CABG; SVST: Single vessel small thoracotomy; MVST: Multiple vessel small thoracotomy; THORACAB: Thoracotomy CABG; MVR: Mitral valve replacement; LEAR: Lateral endoscopic approach with robotics; PFO: Patent foramen ovale; LA: Left atrial; TEASD-R: Totally endoscopic ASP repair; ASD: Atrial septal defect.*

Comorbidities, n(%) or Mean(SD)	CABG			MVR	Other	Total
	non-TECAB	TECAB	Total			
Angina	114/140 (81.4%)	340/425 (80%)	621/943 (65.9%)	-	-	621/943 (65.9%)
Hypertension	107/274 (39%)	861/1,151 (74.8%)	1,075/1,803 (59.6%)	1,380/2,911 (47.4%)	-	2,455/4,714 (52.1%)
Diabetes mellitus	565/879 (64.3%)	294/1,151 (25.5%)	981/2,408 (40.7%)	164/2,929 (5.6%)	-	1,144/5,337 (21.4%)
Dyslipidemia	63/274 (23%)	839/1,117 (75.1%)	902/1,391 (64.8%)	46/203 (22.7%)	-	948/1,594 (59.5%)
Smoking	70/184 (38%)	399/1,151 (34.7%)	536/1,603 (33.4%)	21/68 (30.8%)	-	557/1,671 (33.3%)
CVD	86/879 (9.8%)	49/880 (5.6%)	151/1,869 (8%)	109/2,795 (3.9%)	-	260/4,664 (5.6%)
PVD	59/739 (8%)	37/1,051 (3.5%)	117/1,887 (6.2%)	16/1,231 (1.3%)	-	133/2,418 (5.5%)
COPD	39/739 (5.3%)	122/825 (14.8%)	197/1,942 (10.1%)	92/2,556 (3.6%)	-	289/4,498 (6.4%)
euroSCORE	3.2	1.9	2.3	2.7	0.8	2.5
Pre-operative EF (%)	64.9	66.6	61.3	60.7	-	61
History of MI	44/274 (16%)	274/871 (31.5%)	359/1,413 (25,4%)	17/1,133 (1.5%)	-	375/2,516 (14.9%)
Previous PCI	27/380 (7.1%)	421/1,379 (30.5%)	486/1,869 (26%)	5/417 (1.2%)	-	491/2,286 (21.5%)
Single vessel disease	245/274 (89.4%)	794/1,099 (72.3%)	1,039/1,373 (75.7%)	-	-	1,039/1,373 (75.7%)

Table 2. Comorbidities of the eligible patients according to the type of surgery.

**SD: Standard deviation; CABG: Coronary artery bypass; TECAB: Totally endoscopic CABG; MVR: Mitral valve repair; CVD: Cerebrovascular disease; PVD: Peripheral vascular disease; COPD: Chronic obstructive pulmonary disease; EF: Ejection fraction; MI: Myocardial infarction; PCI: Percutaneous coronary intervention*

Peri-operative data	CABG			MVR	Other	Total
	non-TECAB	TECAB	Total			
Intra-operative data, n(%)						
Total operating time (min)	218	291.7	249.9	256.9	-	253.4
Ventilation time (h)	10.1	12.9	9.9	32.1	-	21.1
CPB time (min)	-	94.9	87.3	133.3	120.5	110.7
XC time (min)	38	67.5	61.3	90.5	48.5	75.7
On-pump, n(%)	1/44 (2.3%)	507/828 (61.2%)	508/872 (58.3%)	-	-	1,009/1,700 (59.4%)
Conversion to open, n(%)	63/980 (6.4%)	97/1,099 (8.8%)	173/2,442 (7%)	58/1,234 (4.7%)	0	231/3,676 (6.3%)
ICU Stay (h)	30.2	27	28.5	29.8	24.5	29.1
LoS (d)	5.1	5.5	5.2	6.5	5.6	5.9
Post-operative data, n(%)						
Bleeding	15/980 (1.5%)	17/994 (1.7%)	38/2,352 (1.6%)	50/2,940 (1.7%)	0/33 (0)	88/5,328 (1.7%)
MI	9/925 (1%)	21/1394 (1.5%)	30/2,587 (1.2%)	9/2,973 (0.3%)	0/33 (0)	39/5,596 (0.7%)
AF	54/824 (6.6%)	80/1,345 (5.9%)	134/2,437 (5.5%)	373/2,973 (12.5%)	0/33 (0)	507/5,446 (9.3%)
CVA	11/925 (1.2%)	14/1,404 (1%)	25/2,597 (1%)	29/2,950 (0.9%)	0/33 (0)	54/5,613 (1%)
Pneumonia	7/925 (0.8%)	29/1,404 (2%)	36/2,707 (1.3%)	3/2,930 (0.1%)	0/33 (0)	39/5,703 (0.7%)
Renal failure	0/925 (0)	10/1,404 (0.7%)	11/2,707 (0.4%)	22/2,930 (0.8%)	0/33 (0)	33/5,703 (0.6%)
Infection	1/925 (0.1%)	5/1,404 (0.4%)	7/2,707 (0.3%)	17/2,950 (0.6%)	0/33 (0)	24/5,723 (0.4%)
Re-operation	13/925 (1.4%)	11/1,404 (0.8%)	27/2,707 (1%)	76/2,950 (2.6%)	0/33 (0)	103/5,723 (1.8%)
30-day Mortality	3/1,065 (0.3%)	14/1,504 (0.9%)	18/2,947 (0.6%)	26/2,993 (0.8%)	0/53 (0)	44/5,933 (0.7%)

Table 3. Intra-operative and post-operative data and 30-day mortality of the included patients that underwent either type of robotic cardiac surgery.
**CABG: Coronary artery bypass; TECAB: Totally endoscopic CABG; MVR: Mitral valve repair; CPB: Cardiopulmonary bypass; XC: Crossclamp; ICU: Intensive care unit; LoS: Length of stay; MI: Myocardial infarction; AF: Atrial fibrillation; CVA: Cerebrovascular accident*

Follow-up data	CABG			MVR	Other	Total
	non-TECAB	TECAB	Total			
Late Mortality, n(%)	12/370 (3.2%)	33/1,403 (2.4%)	26/2,410 (1%)	6/1,659 (0.4%)	0/19	32/4,088 (0.8%)
Late Re-intervention, n(%)	11/1,065 (1%)	15/1,177(1.3%)	26/2,510 (1%)	62/1,915 (3.2%)	0/19	88/4,444 (2%)
MACCE, n(%)	4/129 (3.1%)	168/1,244 (13.5%)	181/1,751 (10.3%)	36/382 (9.4%)	0/19	217/2,152 (10%)
Follow-up duration (mo)	30.1	38.3	36.6	43.5	-	40.1
Follow-up rate (%)	100	99.2	96.4	99.6	-	98

Table 4. Follow-up data and late mortality of the patients that underwent robotic cardiac surgery regarding the type of surgery.

**CABG: Coronary artery bypass; TECAB: Totally endoscopic CABG; MVR: Mitral valve repair; MACCE: Major adverse cardiac and cerebrovascular events*

Appendix B

Tarola	**Tarola, C. L. *et al.* Ultrafast Track Robotic-Assisted Minimally Invasive Coronary Artery Surgical Revascularization. *Innov. Phila. Pa* 12, 346–350 (2017).**
Yang	Yang, M. *et al.* Robotic Total Arterial Off-Pump Coronary Artery Bypass Grafting: Seven-Year Single-Center Experience and Long-Term Follow-Up of Graft Patency. *Ann. Thorac. Surg.* **100,** 1367–1373 (2015).
Wiedeman	Wiedemann, D. *et al.* Robotic totally endoscopic coronary artery bypass grafting in men and women: are there sex differences in outcome? *Ann. Thorac. Surg.* **96,** 1643–1647 (2013).
de Canniere	de Cannière, D. *et al.* Feasibility, safety, and efficacy of totally endoscopic coronary artery bypass grafting: multicenter European experience. *J. Thorac. Cardiovasc. Surg.* **134,** 710–716 (2007).
Dogan	Dogan, S. *et al.* Totally endoscopic coronary artery bypass grafting on cardiopulmonary bypass with robotically enhanced telemanipulation: report of forty-five cases. *J. Thorac. Cardiovasc. Surg.* **123,** 1125–1131 (2002).
Kappert	Kappert, U. *et al.* Robotic coronary artery surgery--the evolution of a new minimally invasive approach in coronary artery surgery. *Thorac. Cardiovasc. Surg.* **48,** 193–197 (2000).
Giambruno	Giambruno, V., Chu, M. W., Cucchietti, C., Boyd, D. W. & Kiaii, B. Robotic-assisted coronary artery bypass surgery: an 18-year single-centre experience. *Int. J. Med. Robot. Comput. Assist. Surg. MRCAS* (2018). doi:10.1002/rcs.1891
Kofler	Kofler, M. *et al.* Robotic Versus Conventional Coronary Artery Bypass Grafting: Direct Comparison of Long-Term Clinical Outcome. *Innov. Phila. Pa* **12,** 239–246 (2017).
Roubelakis	Roubelakis, A. *et al.* Robotic-enhanced coronary surgery in octogenarians. *Interact. Cardiovasc. Thorac. Surg.* **24,** 384–387 (2017).

Hemli	Hemli, J. M. *et al.* Does body mass index affect outcomes in robotic-assisted coronary artery bypass procedures? *Innov. Phila. Pa* **7,** 350–353 (2012).
Bonatti	Bonatti, J. O. *et al.* Hybrid coronary revascularization using robotic totally endoscopic surgery: perioperative outcomes and 5-year results. *Ann. Thorac. Surg.* **94,** 1920–1926; discussion 1926 (2012).
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Supplemental Table 1**.** References of the eligible studies.