Improved Recovery Protocols in Cardiac Surgery: A Systematic Review and Meta-Analysis of Observational and Quasi-Experimental Studies

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ABSTRACT

INTRODUCTION Improved recovery protocols were implemented in surgical specialties over the last decade, which decreased anesthetic and surgical stress and the incidence of perioperative complications. However, these recovery protocols were introduced more slowly for cardiac surgeries. The most frequent complications in cardiac surgery are related to patient clinical status and the characteristics of the surgical procedures involved, which are becoming more varied and complex every day. The first version of the enhanced recovery program for cardiac surgery was published in 2019, but its recommendations were based on only a few studies, and scant research has evaluated its implementation. Randomized and controlled clinical trials for these protocols are scarce, so research that summarizes the results of studies with other methodological designs are useful in demonstrating their benefits in cardiovascular surgery services in Cuba and in other limited-resource settings.

OBJECTIVE Estimate the effectiveness of improved recovery protocols in the perioperative evolution of patients undergoing cardiac surgery.

METHODS We performed a systematic review and meta-analysis according to the guidelines of manual 5.1.0 for reviews of the Cochrane library. We included observational and quasi-experimental studies published from January 2015 through May 2020 that compared enhanced recovery protocols with conventional treatments in patients older than 18 years, and used a quality score to evaluate them. We used the following sources: the Cochrane Library, PubMed, LILACS, SciELO, EBSCO, Google Scholar, Web of Science, Clinical Key, ResearchGate and HINARI. The following keywords were used for the database searches in English: ERAS, protocols and cardiac surgery, enhanced recovery after cardiac surgery, ERACS, clinical pathway recovery and cardiac surgery, perioperative care and cardiac surgery. We used the following search terms for databases in Spanish: *protocolos de recuperación precoz* and *cirugía cardiaca, protocolos de recuperación mejorada* and *cirugía cardiaca, cuidados perioperatorios* and *cirugía cardiaca, programas de recuperación precoz* and *cirugía cardiovascular*. Methodological quality of included investigations was evaluated using the surgical research methodology scale. Meta-analyses were performed for perioperative complications, intensive care unit and hospital stays, and hospital readmission within 30 days of surgery. We calculated effect sizes of the interventions and the corresponding 95% confidence intervals. We used mean differences and confidence intervals for continuous variables, and for qualitative variables we calculated relative risk (RR). Random effects analysis was used. Heterogeneity of the studies was assessed using the Q statistic and the I^2 statistic.

RESULTS We selected 15 studies (a total of 5059 patients: study group, n = 1706; control group, n = 3353). The average quality score for the 15 articles included was 18.9 (out of a maximum of 36 according to the scale) and 66.6% had a score ≥18. With improved recovery protocols in cardiac surgery, the incidence of perioperative complications decreased (RR = 0.73; 95% CI 0.52–0.98) as did hospital readmission within 30 days after surgery (RR = 0.51; 95% CI 95% CI: 0.31–0.86). Differences in extubation time, hospital stay and length of stay in intensive care units were less marked, but always favored the group in which the enhanced protocols were implemented.

CONCLUSIONS Improved recovery protocols in cardiac surgery increase quality of care evidenced by reductions in perioperative complications and decreased incidence of hospital readmission in the month following surgery.

KEYWORDS Enhanced recovery after surgery, rehabilitation, perioperative care, thoracic surgery, cardiac surgical procedures, systematic review, meta-analysis, Cuba

INTRODUCTION

In the last decade, improved recovery protocols were introduced in the surgical clinics of various specialties, which decreased anesthetic and surgical stress, as well as incidence of perioperative complications and morbidity; but their use in heart surgery has been slower despite the obvious advantages. In cardiac surgical procedures, the most frequent complications are related to patient clinical status, including comorbidities, and to increasingly complex and varied surgical procedures. The multimodal, multidisciplinary and continued-care approach of these protocols—which are applied before, during and after surgery—aim to improve quality of care and perioperative evolution, and to aid in early recovery.[1]

IMPORTANCE This study provides evidence pointing to benefits of improved recovery protocols in cardiac surgery, which may lead to their implementation in Cuban heart surgery units and those of hospitals in limited-resource settings.

Patients who undergo cardiac surgery are exposed to events and procedures that can become risk factors for increased morbidity and mortality, including but not limited to: progressive deterioration of nutritional status due to decreasing daily intake and preoperative fasting; anticoagulation procedures during the intraoperative period; prolonged periods of aortic clamping and cardiac arrest; extracorporeal circulation including the potential development of an inflammatory response syndrome; blood transfusions; intensive pharmacological support or mechanical support for low-output syndrome; and late postoperative nutritional support.[1–3] Improved recovery protocols propose comprehensive treatment with actions that cover the entire perioperative period and are designed to ameliorate the negative effects of these factors, and hence they are recommended for implementation in cardiac surgery units.

In 2002, Henrik Kehlet introduced the concept of enhanced recovery protocols (ERAS), and from his work the international non-profit society Enhanced Recovery After Surgery Society (ERASS) was created.[3–6] These programs were applied first in colorectal surgery, and later extended and adapted to other surgical specialties.[4,6–11] The main objective of ERAS protocols is that patients arrive at the surgical procedure in the best clinical conditions possible and that they remain so during and after surgery until discharge via preoperative, intraoperative and postoperative interventions.[7,8,11–15]

ERAS was slow to be introduced into cardiac surgery compared to some other surgical specialties due to the complexity of procedures, differences in conditions required for each intervention, and wide diversity of patient clinical characteristics.[3,16] The first enhanced recovery programs in cardiovascular surgical procedures were the so-called fast-track and ultra-fast track programs, introduced in the 1990s.[17–19] These proposed shortening the duration of orotracheal extubation and postoperative ventilation mechanics, which are risk factors for respiratory complications, as well as shortened stays in hospitals and intensive care units (ICUs). But these actions were focused on a single stage of the perioperative period and were not multidisciplinary. In cardiac surgery, such fast-track and ultra fast-track programs are not applied to all cardiac surgical procedures or to all patients.[17,19–26]

Between 2017 and 2019, publications on the results of ERAS programs in cardiac surgery increased.[6,14,19,23,27–33] World leaders in the specialty recognized the need to adapt the original ERAS programs to cardiac surgery patient characteristics and to each type of intervention, and to generalize a protocol based on the best scientific evidence.[2,14,34,35] The first cardio-surgical symposium for development, evaluation and control of enhanced recovery protocols was held in 2017, whereas ERAS experts published the first ERAS guidelines for cardiac surgery in March 2019,[34,36,37] collectively known as 'ERACS protocols or guidelines'.

These ERACS guidelines have the following characteristics: in the preoperative stage, they propose to educate patients and family members, stratify and control nutritional status, estimate blood glucose levels using glycosylated hemoglobin, eliminate risk factors (tobacco and alcohol), treat infections with prophylaxis, administer carbohydrates two hours before surgery, detect kidney dysfunction early and decrease fasting time (six hours for solids and two to four hours for clear liquids). For the intraoperative period, they propose performing antifibrinolytic therapy with tranexamic acid or Epsilon aminocaproic acid, using multimodal anesthetic and analgesic techniques involving minimal opioids, administering fluids according to hemodynamic variables, controlling hypothermia, maintaining glycemic control, implementing prophylaxis of acute kidney injury and of infections, and using a plate for rigid sternal fixation. For postoperative recovery, they recommend intensively controlling blood glucose levels via continuous infusion, removing dressings from wounds at 48 hours, maintaining thromboprophylaxis, preventing hypothermia, treating pain with minimal use of opioids, stratifying and controlling postoperative delirium, treating acute kidney injury prophylactically, and extubating within the first 6 hours after surgery.[37]

Despite progress in introducing these programs for heart surgery, the authors of the first guidelines concluded that there was not enough published research on the subject, and not enough sound evidence such as that provided by randomized controlled clinical trials (RCTs) and systematic reviews or meta-analyses. Guidelines were issued when there were enough studies to support the introduction of therapeutic measures and diagnostic means.[37]

Evidence-based clinical practice is related to better quality of patient care and improvements in major hospital indicators, and so systematic reviews have gained more followers than detractors and have come to be seen in recent decades as essential tools in developing evidence-based medicine. The validity of individual studies is increased through systematic reviews and areas of controversy are identified where it is necessary to update information and build consensus.[38,39]

At the cardiac unit of the Hermanos Ameijeiras Clinical–Surgical Hospital (HHA) in Havana, Cuba, the first RCT (retrospective record dated 06/09/2012, code RPCEC00000131) was carried out on enhanced recovery in cardiac surgery, with fast-track and multimodal anesthetic methods (association of spinal regional anesthetic techniques with general anesthesia) in myocardial revascularization surgery without extracorporeal circulation. As a result of this RCT,[18] our practice experienced better results during perioperative analgesia, lower doses of systemic opioids were used, the time of mechanical ventilation in the postoperative period was reduced to less than four hours, and incidence of perioperative complications and postoperative stays in hospitals and ICUs decreased. This was the first step in implementing anesthesia strategies based on the best clinical evidence for optimizing patient recovery.[40]

Controversies persist on the benefits of multimodal anesthesia methods that include spinal regional anesthetic techniques in cardiac surgery, because some studies show that these methods do not reduce morbidity in the 30 days following surgery.[41] The authors of the first international version of the ERACS protocol stated that these methods require further evidence and expert evaluation before formal inclusion in the recommendations.[37]

Currently, data is scarce on the benefits of introducing improved recovery protocols in the perioperative clinical practice of cardiac surgery, so we set out to estimate the effectiveness of applying these protocols in the perioperative evolution of patients older than 18 years of age undergoing cardiac surgery, compared with the conventional protocol, based on the primary results of perioperative complications, length of stay in ICUs and hospitals, and hospital readmission within 30 days after the procedure, through a systematic review of observational and quasi-experimental studies, and a meta-analysis.

These programs are useful in focusing on surgical patient care in a comprehensive manner and improving patient care quality by establishing best practices based on documented evidence.

METHODS

This study is a first approximation based on observational and quasi-experimental methodological designs. We carried out a systematic review according to the recommendations outlined in version 5.1.0 of the Cochrane Handbook for Systematic Reviews of Interventions, and the evaluation criteria of the international guide "Preferred Reporting Items for Systematic Reviews and Meta Analyses" (PRISMA).[42,43]

The protocol for this systematic review has been approved by HHA's Scientific Commission (version 0.0, number 2657, May 2018), but it was not registered in electronic databases with national or international access, as is suggested by the PRISMA evaluation guides.[44]

Different meta-analyses were performed for variables of interest whose data were available in three or more of the included studies and whose summary measures were compatible for processing with the EPIDAT 3.1 and Review Manager 5.3 (RevMan 5.3) programs, because all studies did not include the same variables and they needed to be grouped to evaluate those that were both available and of interest.

Search strategy for identifying studies We use the Cochrane Library, PubMed, LILACS, SciELO, EBSCO, Google Scholar, Web of Science, Clinical Key, ResearchGate and HINARI as sources for studies in humans published from January 2015 through May 2020, in both Spanish and English.

The following search terms were used: For databases in English, ERAS; protocols and cardiac surgery; enhanced recovery after cardiac surgery; ERACS; clinical pathway recovery and cardiac surgery; perioperative care and cardiac surgery. For databases in Spanish: *protocolos de recuperación precoz* and *cirugía cardiaca; protocolos de recuperación mejorada* and *cirugía cardiaca; cuidados preoperatorios* and *cirugía cardiaca; programas de recuperación precoz* and *cirugía cardiovascular.*

The search syntax in PubMed, the database that contributed the most references, was as follows:
1. Enhanced recovery AND cardiac surgery
2. Cardiac surgery AND perioperative care
3. Heart surgery AND clinical pathway
4. Perioperative care AND heart surgery
5. # 1 or # 2 or # 3 or # 4

During the first stage, we reviewed titles and abstracts of articles with the potential of meeting study requirements that appeared in the abovementioned search engines. In the second stage, we searched and examined the full texts of the articles selected by title and abstract. Two independent evaluators were used in both stages and discrepancies were discussed. We screened the reference lists of selected articles (a 'search for pearls') to find studies that might be included in the systematic review. We were unable to contact the authors of articles with incomplete information or who presented their information in the form of graphics. An operational model was designed to select studies that included explicit criteria for collecting information. Search results were processed using Zotero 5.0 for Windows bibliographic reference manager.

Criteria for evaluating studies
Study type
1. Observational
2. Quasi-experimental

Participants
Patients aged >18 years scheduled for cardiac surgery with or without extracorporeal circulation (ECC)

Intervention
1. Enhanced recovery protocols or ERACS protocols
2. Conventional protocols

Main outcome measures
Primary or critical outcomes that directly influence decisions
1. Perioperative complications
2. Length of stay in the ICU
3. Length of stay in hospital
4. Hospital readmission within 30 days after surgery
5. Patient satisfaction

Secondary, important, non-critical outcomes that can influence decisions
1. Extubation time
2. Administration of inotropic drugs
3. Early enteral nutrition
4. Early mobilization
5. Total water balance

We did not define these results in the methodology, as definitions may differ between studies, and thus for each study reviewed, we used the same definitions as the researchers.

Exclusion criteria RCTs were excluded, as the purpose of this study was to carry out a systematic review of observational and quasi-experimental investigations for which there were no previous reviews. Studies that did not answer the review questions were also excluded.

Data collection and analysis Two observers collected information independently and selected studies according to the established criteria based on intervention type, participants and outcome measures. When there were discrepancies, a third evaluator was consulted until a consensus was reached. This procedure was followed in the order set forth in the search strategy.

Methodological quality This was assessed for each article using the Methodology of Research in Surgery (MINCIR) scale[45] validated for studies of therapy or therapeutic procedures. This scale consists of three domains: the first assigns scores 1–12 for design type, with the highest score for RCTs, particularly multicenter ones; the second evaluates sample size regardless of the method (or lack thereof) of calculation, and the third is composed of four items, assigning scores of 1–3 to each, which are: quality of the objectives, mention of or justification of the study's design, sample selection criteria (inclusion and exclusion) and whether or not the sample size is justified. The score's total is then 6–36 points. The cut-off value for methodological quality was 8 points, because RCTs were not included, and studies were observational and quasi-experimental. Studies that obtained a score ≥18 were assessed as having good methodological quality, and studies with a score ≤17 points were assessed as having poor methodological quality.

Procedures for meta-analysis Magnitudes of the interventions' effects with their respective 95% confidence intervals (CI) were calculated for the qualitative response variables using relative risk (RR) as a measure of effect, calculated as *risk of event in the ERACS group/risk of event in the control group,* so that higher risks of the event presenting in the control group (CG) produced RRs lower than would have been the case had the two groups been combined. For quantitative variables, the difference in means between the ERACS group and the CG was used as a measure of effect, so that values <0 implied a favorable effect for the intervention. Random effects analyses were used for all variables, since fixed-effect meta-analyses ignore non-random sources of variation between studies. The heterogeneity of the studies was assessed using Q and I^2 statistics. Sensitivity was estimated by the change in the global effect when articles with inadequate or poor methodological quality were eliminated (score ≤17). Publication bias was assessed using the Egger t-test statistic.[42]

RESULTS

The study selection process' exclusion criteria are shown in a flow chart (Figure 1).

The 15 selected articles contributed 5059 patients (ERACS group: n = 1706; CG: n = 3353). The methodological quality of the studies was good. Ten of the 15 articles (66.7%) scored ≥18 points out of a maximum of 36 possible in the MINCIR guide (Table 1).

Meta-analytic comparisons were made between ERACS and conventional interventions for primary outcome variables: perioperative complications, ICU stay, hospital stay, and hospital readmission within 30 days after surgery.

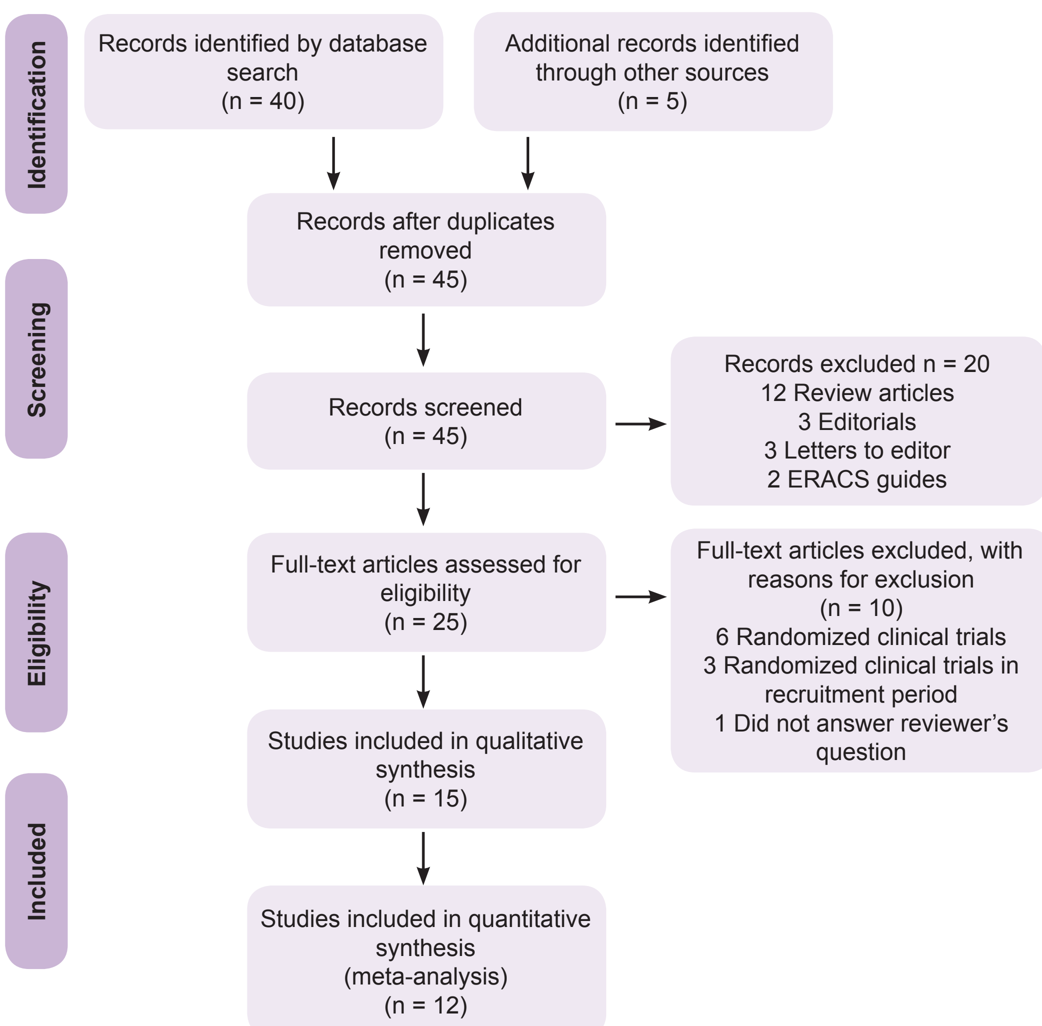
Meta-analysis was performed for perioperative complications in the 12 studies that contained information on this variable (total: n = 937 patients; ERACS: n = 290; CG: n = 647).

A tree graph shows the studies included in this meta-analysis, as well as the overall estimate of the hazard ratios for the randomized studies (Figure 2). ERACS protocols were associated with a lower incidence of complications with a RR <1 in the random effect analysis (RR = 0.72; 95% CI: 0.52–0.98). Heterogeneity was significant ($p < 0.001$; Q statistic = 43.30; I^2 statistic = 75%). Publication bias was significant (p = 0.04; Egger's test, Z statistic = 2.10).

We analyzed the 3 of 14 studies (21.4%) that evaluated the variable of average ICU stay (Gimpel 2018, Motwani 2019 and Chen 2020; total: n = 1935; ERACS: n = 278; CG: n = 1657). There were no significant differences in the random effects analysis (mean difference = –3.52; 95% CI: –7.16–0.11) although the direction of the effect remained favorable to the ERACS group. Heterogeneity was not significant (p = 0.76; chi-square Q statistic = 468.28) and there was no publication bias (p = 0.76; Egger's test).

For hospital stay, the two groups were compared using 3/15 studies (20.0%) that contained information for this variable (Motwani 2019, Kowalski 2019 and Chen 2020; total n = 880; ERACS n = 441; CG n = 439). The results were similar to those obtained in the ICU stay analysis. No significant differences

Figure 1: Flow diagram according to PRISMA



ERACS: enhanced recovery after cardiac surgery PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Table 1: Basic data and methodological quality of studies

Authors	Year	Total n	ERACS n	Control n	Surgery type	Quality	Reference
Zaouter C, et al.	2015	71	38	33	MRV	20	[27]
Fleming IO, et al.	2016	106	53	53	MRV / VR / MRV+VR	23	[35]
van der Kolk M, et al.	2017	243	81	162	MRV / VR / MRV+VR	28	[30]
Martinos C, et al.	2017	100	100		MRV / VR / MRV+VR	11	[46]
Motwani SK, et al.	2019	133	63	70	MRV/VR/Myxomas	21	[47]
Gimpel D, et al.	2018	1717	168	1549	MRV /VR / MRV+VR	18	[48]
Markham T, et al.	2019	50	25	25	RVM	19	[49]
Williams JB, et al.	2019	973	443	530	MRV / VR	20	[50]
Grant MC, et al.	2019	315	84	231	MRV / VR/ MRV+VR	18	[51]
Zaouter C, et al.	2019	46	23	23	AVR. Min. Invasive	20	[52]
Varelmann D, et al.	2019	280	107	173	MRV /VR/ MRV+VR	17	[53]
Zammert M, et al.	2019	212	115	97	-----------	17	[54]
Kowalski S, et al.	2019	662	331	331	MRV / VR / MRV+VR	16	[55]
Borys M, et al.	2020	57	28	29	MRV w/out ECC	14	[56]
Chen L, et al.	2020	94	47	47	MRV w/out ECC	22	[57]
Total		5059	1706	3353		18.93	

*Type of surgical procedure was not reported.
AVR: aortic valve replacement; ECC: extracorporeal circulation; ERACS: enhanced recovery after cardiac surgery;
MRV: myocardial revascularization; VR: valve replacement

were found between the groups with the random effects analysis, but despite this, the direction of the measured effect favored the ERACS group (combined mean difference = –0.81; 95% CI: –2.13–0.51). Heterogeneity was significant (p <0.001; chi-square Q statistic = 95.19). There was no publication bias for this outcome according to Egger's test (p = 0.49).

We performed a meta-analysis using 6 of the 7 studies that addressed hospital readmission in the first 30 days after surgery (van der Kolk 2017, Gimpel 2018, Motwani 2019, Zaouter 2019, Zammert 2019 and Kowalski 2019; n = 3195; ERACS n = 881; CG n = 2314) (Figure 3). In the random effects analysis there were significant differences in favor of the ERACS group (RR = 0.51; 95% CI: 0.31–0.86). Heterogeneity was not significant (p = 0.27, Q chi-square statistic = 6.41, I^2 statistic = 22%), but publication bias was significant according to Egger's test (p = 0.01).

Meta-analytic comparisons were made with secondary endpoints for extubation time and inotropic drug administration.

For extubation time, a meta-analysis was performed using 3/11 studies that reported the variable (Zaouter 2015, Motwani 2019, Chen 2020; n = 289; ERACS n = 148, CG n = 141) (Figure 4). There were no significant differences in the random effect analysis; even so, the direction of the mean effect favors the ERACS group (mean difference –114.98; 95% CI: –278.74–48.78). There was heterogeneity, demonstrated in the graph with high chi-square values and very low p values, in addition to the value of the I^2 statistic. Egger's test for detecting of publication bias was not significant at p = 0.02.

There were no significant differences between the groups when assessing administration of inotropic drugs (RR = 1.34; 95% CI: 0.87–2.07). Heterogeneity was significant (p = 0.04; Q chi-square statistic = 6.37), but publication bias was not (p = 0.29).

There were no substantial changes in significance in the sensitivity analysis for the six meta-analytic comparisons, and confidence intervals were of very similar widths.

Figure 2: Perioperative complications, random effect

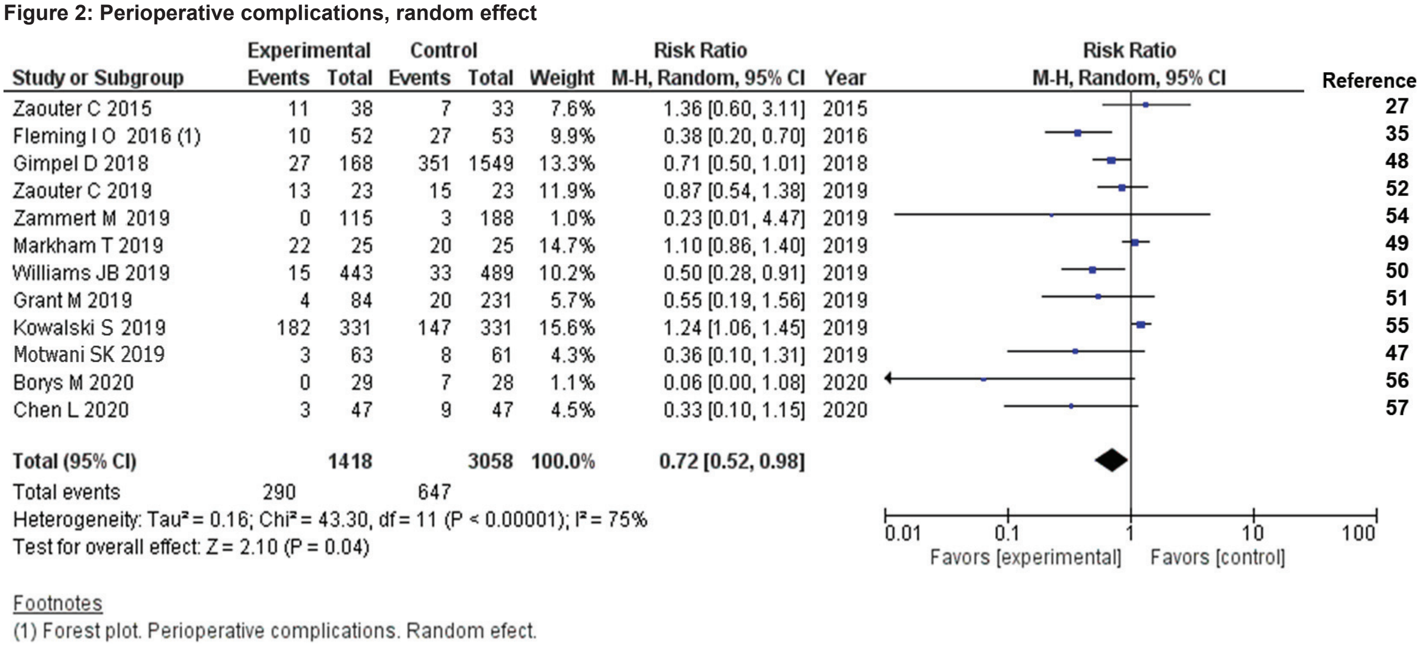


Figure 3: Hospital readmission, random effect

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI	Year	Reference
van der Kolk M 2017	3	81	13	162	14.5%	0.46 [0.14, 1.57]	2017	30
Martinos C 2017	6	100	0	0		Not estimable	2017	46
Gimpel D 2018	9	168	183	1549	34.7%	0.45 [0.24, 0.87]	2018	48
Zammert M 2019	10	115	15	188	28.6%	1.09 [0.51, 2.34]	2019	54
Motwani SK 2019	3	63	8	61	13.5%	0.36 [0.10, 1.31]	2019	47
Kowalski S 2019	1	331	8	331	5.8%	0.13 [0.02, 0.99]	2019	55
Zaouter C 2019	0	23	2	23	2.9%	0.20 [0.01, 3.95]	2019	52
Total (95% CI)		**881**		**2314**	**100.0%**	**0.51 [0.31, 0.86]**		
Total events	32		229					

Heterogeneity: Tau² = 0.09; Chi² = 6.41, df = 5 (P = 0.27); I² = 22%
Test for overall effect: Z = 2.52 (P = 0.01)

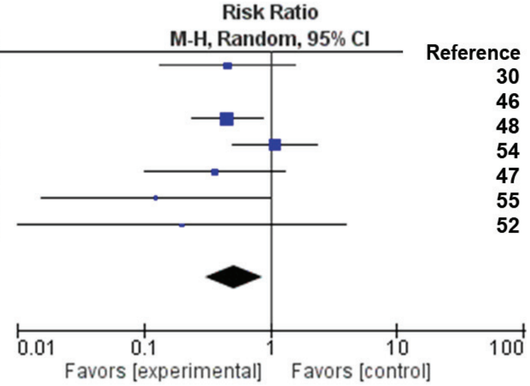
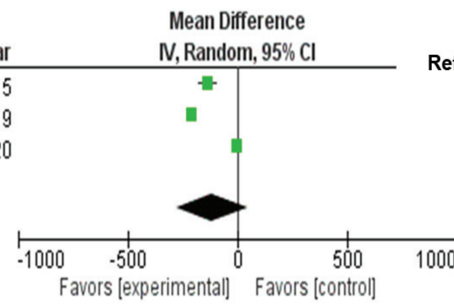


Figure 4: Extubation time (in minutes), random effect

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI	Year	Reference
Zaouter C 2015	21	8	38	157	113	33	32.9%	-136.00 [-174.64, -97.36]	2015	27
Motwani SK 2019	60.26	19.96	63	268.54	28.15	61	33.5%	-208.28 [-216.89, -199.67]	2019	47
Chen L 2020	7.59	1.93	47	8.72	6.35	47	33.5%	-1.13 [-3.03, 0.77]	2020	57
Total (95% CI)			**148**			**141**	**100.0%**	**-114.98 [-278.74, 48.78]**		

Heterogeneity: Tau² = 20809.19; Chi² = 2159.20, df = 2 (P < 0.00001); I² = 100%
Test for overall effect: Z = 1.38 (P = 0.17)



DISCUSSION

Enhanced recovery and success of complex surgeries like cardiac surgery depend on interventions guided by evidence-based protocols on the reduction of perioperative complications, length of stays in hospitals and ICUs, and readmission to the hospital after discharge.

Our analysis, which reviews studies from varied settings, confirms that ERACS program quality depends primarily on provider experience and patient selection and preparation (as outlined in ERACS protocols), and not necessarily on available material resources of individual cardiac surgery units, which allows these programs to be implemented in limited-resource settings.

The choice of including only observational or quasi-experimental studies in this review that commonly incorporate a greater number of response variables and that had not been included in previous systematic reviews may have decreased the sensitivity of some statistical contrasts, but the exclusion of RCTs did not lead to publication bias.

There are no reports of systematic reviews accompanied by meta-analyses comparing ERACS protocols with conventional procedures for cardiac surgery. One study, published in 2018,[58] evaluates the effectiveness of fast-track programs in cardiac surgical procedures. Through individual analysis of seven investigations, the authors concluded that these programs reduce postoperative mechanical ventilation time, ICU stays and costs when implemented in well-selected patients.

In the studies we included, incidence of perioperative complications decreased with ERACS protocols compared to traditional methods of preparing patients for general anesthesia, also associated with a decrease in hospital readmission in the 30 days after surgery, indicating the advantages of these protocols in improving surgical patient quality of care. The differences for ICU and hospital stays and for extubation time after surgery were smaller, but always favored the ERACS group. No improvement was seen in the ERACS group for inotropic drug administration.

Heterogeneity tests were significant in half of the meta-analyses performed, which can be attributed to different procedures (valve replacement or repair, excision of intracardiac tumors) and surgical techniques (cardiac surgery with and without extracorporeal circulation) included in the analysis. This made it difficult to integrate evidence from studies conducted in different settings, with varied designs, and that included subjects with different clinical diagnoses and different surgical procedures and techniques.[42] The sensitivity analysis showed that eliminating studies with lower evidence quality (higher risk of bias) did not change the basic results, which lends them more credit.

A limitation of the research is publication bias in some of the meta-analyses. This may be due to the fact that few studies were included in the meta-analyses, due to strict inclusion criteria. Another limitation was the incompatibility of the metric criteria in several of the studies with those commonly used in software available for meta-analyses.

Although the scales recommended to assess methodological quality of articles[43,44] are the Newcastle–Ottawa scale,[59] the Strengthening the Reporting of Observational studies in Epidemiology (STROBE),[60] or the Quality Assessment Tool for Systematic Reviews of Observational Studies guide

(QATSO),[61] we opted for the MINCIR scale,[45] which is not limited to assessing presence or absence of attributes in articles, but also assesses quality of information presented.

Several confidence intervals for parameters of interest were considerably wide, and therefore unreliable, due to small sample sizes.[62] This circumstance does not call into question the results but reveals the need for more original studies on the implementation of ERACS protocols in cardiac surgery.

CONCLUSIONS

Improved recovery protocols in cardiac surgery reduce perioperative complications in patients and decrease the incidence of hospital readmission in the 30 days after surgery, and also reduce the length of stays in intensive care units and hospitals. The study is an important, although preliminary, step to establish the usefulness of ERAS protocols in anesthesiology and cardiac surgery, as it summarizes variables that are hospital system indicators that relate to hospital performance and quality of care.

REFERENCES

1. Pajares MA, Margarit JA, García-Camacho C, García-Suárez J, Mateo E, Castaño M, et al. DOCUMENTO DE CONSENSO Vía clínica de recuperación intensificada en cirugía cardiaca. Documento de consenso de la Sociedad Española de Anestesiología, Reanimación y Terapéutica del Dolor (SEDAR), la Sociedad Española de Cirugía Cardiovascular y Endovascular (SECCE) y la Asociación Española de Perfusionistas (AEP). Rev Esp Anestesiol Reanim [Internet]. 2021 Apr [cited 2021 May 2];68(4):183–231. Available at: https://doi.org/10.1016/j.redar.2020.11.005. Spanish, English.
2. Agüero Martínez MO. Protocolos de recuperación mejorada en cirugía cardiaca: aspectos esenciales de la evaluación y el apoyo nutricional perioperatorio. Rev Cub Anest Rean [Internet]. 2019 May–Aug [cited 2019 Aug 5];18(2):e496. Available at: http://www.revanestesia.sld.cu/index.php/anestRean/article/view/496/816. Spanish.
3. Agüero Martínez MO. Protocolos de recuperación precoz en cirugía cardiaca. ¿Utopía o realidad? Rev Cub Anest Rean [Internet]. 2018 May–Aug [cited 2018 Dec 26];17(2):42–52. Available at: http://www.revanestesia.sld.cu/index.php/anestRean/article/view/415/426. Spanish.
4. Ljungqvist O, Young-Fadok T, Demartines N. The history of Enhanced Recovery After Surgery and the ERAS Society. J Laparoendosc Adv Surg Tech. 2017 Sep;27(9):860–2.
5. Melnyk M, Casey RG, Black P, Koupparis AJ. Enhanced Recovery After Surgery (ERAS) protocols: time to change practice? Can Urol Assoc J [Internet]. 2011 Oct [cited 2018 Jan 13];5(5):342–8. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/22031616/
6. Senturk J, Kristo G, Gold J, Bleday R, Whang E. The development of Enhanced Recovery After Surgery across surgical specialties. J Laparoendosc Adv Surg Tech A. 2017 Sep;27(9):863–70.
7. Lau CSM, Chanberlain RS. Enhanced recovery after surgery programs improve patient outcomes and recovery: a meta-analysis. World J Surg [Internet]. 2017 Apr [cited 2018 Jan 13];41(4):899–913. Available at: https://doi.org/10.1007%2Fs00268-016-3807-4
8. Scarci M, Solli P, Bedetti B. Enhanced recovery pathway for thoracic surgery in the UK. J Thorac Dis [Internet]. 2016 Feb [cited 2018 Jan 11];8(Suppl 1):S78–83. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/26941974/
9. Lujungqvist O, Thanh NX, Nelson G. ERAS valued-based surgery. Review article. J Surg Oncol [Internet]. 2017 Oct [cited 2018 Jan 13];116(5):608–12. Available at: https://doi.org/10.1002/jso.24820
10. Manso M, Schemelz J, Aloia T. ERAS- Anticipated outcomes and realistic goals. J Surg Oncol [Internet]. 2017 Oct 1 [cited 2018 Jan 13];116(5)570–7. Available at: https://doi.org/10.1002%2Fjso.24791
11. Soeters PB. The Enhanced Recovery After Surgery (ERAS) program: benefit and concerns. Am J Clin Nutr [Internet]. 2017 Jul [cited 2018 Jan 13];106(1):10–1. Available at: https://doi.g/10.3945%2Fajcn.117.159897
12. Roulin D, Najjar P, Demartines N. Enhanced Recovery After Surgery implementation: from planning to success. J Laparoendosc Adv Surg Tech A. 2017 Sep;27(9):876–9.
13. Abeles A, Kwasnicki RM, Darzi A. Enhanced recovery after surgery: Current research insights and future direction. World J Gastrointest Surg [Internet]. 2017 Feb 27 [cited 2018 Jan 13];9(2):37–45. Available at: https://doi.org/10.4240%2Fwjgs.v9.i2.37
14. Indraratna K. A proposed strategy for enhanced recovery after cardiac surgery. Surgery Curr Res [Internet]. 2017 Sep [cited 2018 Jan 11];7(5 Suppl). Available at: https://doi.org/10.4172%2F2161-1076-C1-032
15. Nanavati AJ, Prabhakar S. Enhanced Recovery After Surgery: if you are not implementing it, why not? Practical Gastroenterol Series [Internet]. 2016 Apr [cited 2018 Jan 13];151:46–56. Available at: http://www.practicalgastro.com
16. Agüero Martínez MO. Protocolos de recuperación precoz en cirugía cardiaca. Evidencias en la práctica clínica. In: Centro de Eventos ORTOP: ECIMED. Jornada Habana 500 y III Taller Nacional de anestesia Obstétrica [Internet]. Havana: ECIMED; 2019 [cited 2019 Nov 1]. Available at: http://actasdecongreso.sld.cu/index.php?P=FullRecord&ID=2523. Spanish.
17. Chaney MA. Intrathecal and epidural anesthesia and analgesia for cardiac surgery. Anesth Analg. 2006 Jan;102(1):45–64.
18. Agüero Martínez MO. Métodos anestésicos multimodales en el procedimiento quirúrgico de revascularización miocárdica sin circulación extracorpórea. Ensayo clínico aleatorizado y meta-análisis [thesis] [Internet]. [Havana]: University of Medical Sciences of Havana, Hermanos Ameijeiras Clinical Surgical Hospital; 2011 [cited 2018 Jan 23]. 130 p. Available at: http://tesis.sld.cu/index.php?P=FullRecord&ID=306. Spanish.
19. Tham YC, Tan Z, Tam ALW, Sharad SS, Sin KYK, Ong KK. Improving on fast- track protocol for post cardiac surgery patients. J Cardiothorac Surg [Internet]. 2015 Dec 16 [cited 2018 Jan 11];10(Suppl 1):A330. Available at: https://doi.org/10.1186%2F1749-8090-10-S1-A330
20. Liu SS, Block BM, Wu CL. Effects of perioperative central neuraxial analgesia on outcome after coronary artery bypass surgery. A meta-analysis. Anesthesiology. 2004 Jul;101(1):153–61.
21. Hejimans JH, Lancé MD. Fast track minimally invasive aortic valve surgery: patient selection and optimizing. Eur Heart J Suppl [Internet]. 2017 Jan [cited 2018 Jan 6];19(Suppl A):A8–14. Available at: https://doi.org/10.1093/eurheartj/suw056
22. Lena P, Balarac N, Lena D, De la Chapelle A, Arnulf JJ, Mihoubi A, et al. Fast-track anesthesia with remifentanil and spinal analgesia for cardiac surgery: the effect on pain control and quality of recovery. J Cardiothorac Vasc Anesth. 2008 Aug;22(4):536–42.
23. Jakobsen CJ. High thoracic epidural in cardiac anesthesia: a review. Semin Cardiothorac Vasc Anesth [Internet]. 2015 Mar [cited 2018 Jan 7];19(1):38–48. Available at: https://doi.org/10.1177%2F1089253214548764
24. Moraes dos Santos L, Cavani Jorge Santos V, Cavani Jorge Santos SR, Sá Malbouisson LM. Intrathecal morphine plus general anesthesia in cardiac surgery: effects on pulmonary function, post-operative analgesia and plasma morphine concentration. Clinics (Sao Paulo). 2009;64(4):279–85.
25. Yapici D, Ozer ZO, Atici S, Bilgin E, Doruk N, Cinel I, et al. Postoperative effect of low-dose intrathecal morphine in coronary artery bypass surgery. J Card Surg. 2008 Mar–Apr;23(2):140–5.
26. Tenenbein PK, Debrouwere R, Maguire D, Duke PC, Muirhead B, Enns J, et al. Thoracic epidural analgesia improves pulmonary function in patients undergoing cardiac surgery. Can J Anaesth. 2008 Jun;55(6):344–50.
27. Zaouter C, Imbault J, Labrousse L, Abdelmoumen Y, Coiffic A, Colona G, et al. Association of robotic totally endoscopic coronary artery bypass graft surgery associated with a preliminary cardiac enhanced recovery after surgery. J Cardiothorac Vasc Anesth. 2015 Dec;29(6):1489–97.
28. Ender J, Borger MA, Scholz M, Funkat AK, Anwar N, Sommer M, et al. Cardiac surgery fast-track treatment in a post anesthetic care unit. Anesthesiology. 2008 Jul;109(1):61–6.
29. Tian GJ, Li DY, Dong YD, Peng YN, Liu P, Wei YK, et al. [Clinical efficacy of enhanced recovery after surgery in atrial caval shunting for type A Budd-Chiari syndrome]. Zhonghua Wai Ke Za Zhi. 2017 Sep 1;55(9):671–7. Chinese.
30. van der Kolk M, van den Boogaard M, Brugge-Speeman CT, Hol J, Noyez L. Development and implementation of a clinical pathway for cardiac surgery in the intensive care unit: effects on protocol adherence. J Eval Clin Pract [Internet]. 2017 Dec [cited 2018 Jan 6];23(6):1289–98. Available at: https://doi.org/10.1111%2Fjep.12778
31. Hardman G, Bose A, Saunders H, Walker AH. Enhanced recovery in cardiac surgery. J Cardiothorac Surg [Internet]. 2015 [cited 2018 Jan 11];10(Suppl 1):A75. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4693802/
32. Anastasiadis K, Asterious C, Antonitsis P, Agiriadou H, Grosomannidis V, Kyparissa M, et al. Enhanced recovery after elective coronary revascularization surgery with minimal versus conventional extracorporeal circulation: a prospective randomized study. J Cardiothorac Vasc Anesth [Internet]. 2013 Oct [cited 2018 Jan 11];27(5):859–64. Available at: https://linkinghub.elsevier.com/retrieve/pii/S1053-0770(13)00018-9
33. Waite I, Deshpande R, Baghai M, Massey T, Wendler O, Greenwood S. Home-based preoperative rehabilitation (prehab) to improve physi-

cal function and reduce hospital length of stay for frail patient undergoing coronary artery bypass graft and valve surgery. J Cardiothorac Surg. 2017 Oct 26;12(1):91.

34. Morasch A. 1st ERACS Best Practices Symposium. The formation of Enhanced Recovery After Cardiac Surgery Society. Enhanced Recovery After Cardiac Surgery Society [Internet]. 2017 [cited 2018 Jan 14]. Available at: http://www.eracs.org
35. Fleming IO, Garratt C, Guha R, Desai J, Chaubey S, Wang Y, et al. Aggregation of marginal gains in cardiac surgery: feasibility of a perioperative care bundle for enhanced recovery in cardiac surgical patient. J Cardiothorac Vasc Anesth [Internet]. 2016 Jun [cited 2018 Jan 14];30(3):665–70. Available at: https://linkinghub.elsevier.com/retrieve/pii/S1053-0770(16)00022-7
36. Williams P. ERAS Cardiac Surgery Named Official Heart Surgery Representative for ERAS Society [Internet]. San Francisco: Businesswire; 2018 Apr 12 [cited 2018 Sep 9]. Available at: https://www.businesswire.com/news/home/20180412005503/en/ERAS-Cardiac-Surgery-Named-Official-Heart-Surgery
37. Engelman DT, Ben Ali W, Williams JB, Perrault LP, Reddy VS, Arora RC, et al. Guidelines for perioperative care in cardiac surgery: Enhanced Recovery After Surgery Society recommendations. JAMA Surg [Internet]. 2019 Aug 1 [cited 2019 May 9];154(8):755–66. Available at: https://doi.org/10.1001%2Fjamasurg.2019.1153
38. Ferreira González I, Urrutia G, Alonso-Coello P. Revisiones sistemáticas y meta-análisis: bases conceptuales e interpretación. Rev Esp Cardiol [Internet]. 2011 [cited 2018 May 16];64(8):688–96. Available at: http://www.revespcardiol.org/es/revisiones-sistematicas-metaanalisis-bases-conceptuales/articulo/90024424/. Spanish.
39. Catalá LF, Tobías A, Roqué M. Conceptos básicos del metanálisis en red. Atención Primaria [Internet]. 2014 [cited 2018 May 16];46(10):573–81. Available at: http://www.sciencedirect.com/science/article/pii/S0212656714001218. Spanish.
40. Agüero Martínez MO. Anestesia multimodal en Cirugía cardiovascular. In: Protocolización de la asistencia médica en el Hospital Hermanos Ameijeiras: resultados en los primeros 5 años de aplicación. 1st ed. Havana: ECIMED; 2012. p. 103–9. Spanish.
41. Guay J, Kopp S. Epidural analgesia for adults undergoing cardiac surgery with or without cardiopulmonary bypass. Cochrane Database of Syst Rev [Internet]. 2019 Mar 1 [cited 2019 Sep 3];3(3):CD006715. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/30821845/
42. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions 5.1.0 [Internet]. London: The Cochrane Collaboration; 2011 [updated 2011 Mar; cited 2018 Mar 8]. Available at: https://handbook-5-1.cochrane.org/
43. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA Statement. PLoS Med [Internet]. 2009 [cited 2017 Jan 10];6(7):e1000097. Available at: www.prisma-statement.org/documents/PRISMA%202009%20checklist.pdf
44. Hutton B, Catala-López F, Moher D. La extensión de la declaración PRISMA para revisiones sistemáticas que incorporan metaanálisis en red: PRISMA-NMA. Med Clin (Barc) [Internet]. 2016 [cited 2018 May 16]. Available at: http://www.elsevier.es/en/linksolver/ft/pii/S0025-7753(16)00151-2. Spanish.
45. Moraga J, Manterola C, Cartes-Velásquez RA, Burgos ME, Aravena P, Urrutia S. Instrucciones para la utilización de la escala MINCIR para valorar calidad metodológica de estudios de terapia. Int J Morphol. 2014 May;32(1):294–8. Spanish.
46. Martinos C, Daliakopolous S, Tsakalakis C, Georgiu M, Moraitis S. The use of fast track protocol for perioperative management of cardiac surgery patients. Anesth Crit Care Open Access [Internet]. 2017 Jun 13 [cited 2018 Jan 7];8(2). Available at: https://doi.org/10.15406%2Fjaccoa.2017.08.00301
47. Motwani SK, Yadav VK, Jhanwar S. Enhanced Recovery After Cardiac Surgery - A single tertiary care centre experience in India. EC Anaesthesia. 2019;5(4):97–105.
48. Gimpel D, Shanbhag S, Srivastava T, MacLeod M, Conaglen P, Kerjiwal N, et al. Early discharge from intensive care after cardiac surgery is feasible with an adequate fast track, stepdown unit: Waikato Experience. Heart Lung Circ [Internet]. 2019 Dec [cited 2019 Aug 8];28(12):1888–95. Available at: https://linkinghub.elsevier.com/retrieve/pii/S1443-9506(18)31970-X
49. Markham T, Wegner R, Hernández N, Lee JW, Choi W, Eltzschig HK, et al. Assessment of a multimodal analgesia protocol to allow the implementation of enhanced recovery after cardiac surgery: Retrospective analysis of patient outcomes. J Clin Anaesth [Internet]. 2019 May [cited 2019 Aug 9];54:76–80. Available at: https://www.sciencedirect.com/science/article/abs/pii/S0952818018309747?via%3Dihub
50. Williams JB, McConnell G, Allender JE, Woltz P, Kane K, Smith PK, et al. One-year results from the first US-based enhanced recovery after cardiac surgery (ERAS Cardiac) program. J Thorac Cardiovasc Surg [Internet]. 2019 May [cited 2019 Aug 8];157(5):1881–88. Available at: https://linkinghub.elsevier.com/retrieve/pii/S0022-5223(18)33225-2
51. Grant MC, Isada T, Ruzankin P, Whitman G, Lawton JS, Dodd-O J, et al. Results from an enhanced recovery program for cardiac surgery. J Thorac Cardiovasc Surg [Internet]. 2019 [cited 2019 Aug 8];159(4):1393–1402. Available at: https://linkinghub.elsevier.com/retrieve/pii/S0022-5223(19)31136-5
52. Zaouter C, Oses P, Assatourian S, Labrousse L, Remy A, Ouattara A. Reduced length of hospital stay for cardiac surgery—implementing an optimized perioperative pathway: prospective evaluation of an Enhanced Recovery After Surgery program designed for mini-invasive aortic valve replacement. J Cardiothorac Vasc Anesth [Internet]. 2019 Nov [cited 2019 Aug 8];33(11):3010–19. Available at: https://linkinghub.elsevier.com/retrieve/pii/S1053-0770(19)30462-8
53. Varelmann D, Shook D, Buric D, Yadzchi F, Dinga Madou I, Morth K, et al. Enhanced recovery after cardiac surgery: fluid balance and incidence of acute kidney injury. J Cardiothorac Vasc Anesth [Internet]. 2019 Sep [cited 2019 Nov 14];33 Suppl 2:S140–68. Available at: https://www.sciencedirect.com/science/article/abs/pii/S1053077019306548
54. Zammert M, Buric D, Yazdchi F, Dinga Madou I, Manca C, Woo S, et al. The influence of Enhanced Recovery After Cardiac Surgery on 30-day readmission rate, hospital and ICU length of stay. J Cardiothorac Vasc Anesth. 2019 Sep;33 Suppl 2:S102.
55. Kowalski S, Goldie D, Maguire D, Arora RC, Girling I, Fransoo R, et al. High spinal anesthesia combined with general anesthesia versus general anesthesia alone: a retrospective cohort study in cardiac surgical patients. Acta Anaesth Belg. 2019;70(2):63–70.
56. Borys M, Żurek S, Kurowicki A, Horeczy B, Bielina B, Sejboth J, et al. Implementation of Enhanced Recovery After Surgery (ERAS) protocol in off-pump coronary artery bypass graft surgery. A prospective cohort feasibility study. Anaesthesiol Intensive Ther [Internet]. 2020 Jan [cited 2020 Dec 1];52(1). Available at: https://www.termedia.pl/Implementation-of-Enhanced-Recovery-After-Surgery-ERAS-protocol-in-off-pump-coronary-artery-bypass-graft-surgery-r-nA-prospective-cohort-feasibility-study,118,39938,0,1.html
57. Chen L, Zheng J, Kong D, Yang L. Effect of Enhanced Recovery After Surgery protocol on patients who underwent off-pump coronary artery bypass graft. Asian Nursing Res (Korean Soc Nurs Sci) [Internet]. 2020 Feb [cited 2020 Jan 1];14(1):44–9. Available at: https://linkinghub.elsevier.com/retrieve/pii/S1976-1317(20)30004-9
58. Schulte K, Antoniou A, Attia R. Does fast-track recovery improve outcomes in adult cardiac surgery? Ann Cardiol Vasc Med [Internet]. 2018 Dec [cited 2018 Dec 26];3:1012. Available at: https://www.researchgate.net/publication/330847247_Does_fast-track_recovery_improve_outcomes_in_adult_cardiac_surgery
59. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomised studies in meta-analyses [Internet]. Ottawa: The Ottawa Hospital Research Institute; 2021 [cited 2021 Jan 2]. Available at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
60. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. Declaración de la iniciativa STROBE (Strengthening the Reporting of Observational studies in Epidemiology): directrices para la comunicación de estudios observacionales. Rev Esp Salud Pública. 2008 May–Jun;22(3):251–9. Spanish.
61. Wong WCW, Cheung CSK, Hart GJ. Development of a quality assessment tool for systematic reviews of observational studies (QATSO) of HIV prevalence in men having sex with men and associated risk behaviours. Emerg Themes Epidemiol [Internet]. 2008 Nov 17 [cited 2018 May 5];5:23. Available at: https://ete-online.biomedcentral.com/articles/10.1186/1742-7622-5-23
62. Dagnino SJ. Intervalos de confianza. Rev Chil Anest [Internet]. 2014 [cited 2021 May 15];43(2):129–33. Available at: https://doi.org/10.25237/revchilanestv43n02.11

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