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Survival after Perioperative Cardiopulmonary Resuscitation

Providing an Evidence Base for Ethical Management of Do-not-resuscitate Orders

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ABSTRACT

Automatic suspension of do-not-resuscitate (DNR) orders during general anesthesia does not sufficiently address a patient's right to self-determination and is a practice still observed among anesthesiologists today. To provide an evidence base for ethical management of DNR orders during anesthesia and surgery, the authors performed a systematic review of the literature to quantify the survival after perioperative cardiopulmonary resuscitation (CPR). Results show that the probability of surviving perioperative CPR ranged from 32.0 to 55.7% when measured within the first 24 h after arrest with a neurologically favorable outcome expectancy between 45.3 and 66.8% at follow-up, which suggests a viable survival of approximately 25%. Because CPR generally proves successful in less than 15% of out-of-hospital cardiac arrests, the altered outcome probabilities that the conditions in the operating room bring on warrant reevaluation of DNR orders during the perioperative period. By preoperatively communicating the evidence to patients, they can make better informed decisions while reducing the level of moral distress that anesthesiologists may experience when certain patients decide to retain their DNR orders. (ANESTHESIOLOGY 2016; 124:723-30)

ANESTHESIOLOGISTS frequently face moral distress when they provide anesthesia care to patients with do-not-resuscitate (DNR) orders.[1] Maintenance of cardiorespiratory stability is by many considered central to the function of an anesthesiologist. In this sense, the definition of cardiopulmonary resuscitation (CPR) as the combined set of procedures (consisting of at least chest compressions and/or defibrillation) directed at restoring cardiopulmonary circulation[2] more or less equates to anesthesia care. "Doing nothing when something can be done"[3] can be particularly distressing when there are concerns that the surgical procedure or the administration of anesthetics may have triggered the intraoperative cardiac arrest.

Before the 1990s, DNR orders were routinely suspended during the intraoperative period and immediate postoperative periods.[4,5] In the wake of significant criticism about these practices, the American Society of Anesthesiologists (ASA) created a set of guidelines to endorse a policy of required reconsideration. The guidelines state that "automatically suspending DNR orders or other directives that limit treatment prior to procedures involving anesthetic care may not sufficiently address a patient's rights to self-determination in a responsible and ethical manner."[6] By preoperatively communicating to the patient that the administration of anesthesia may involve some procedures that might be viewed as CPR in other settings, the decision whether to (temporarily) modify any treatment limiting directive is turned into a shared one.

Although a trend toward compliance with professional standards has been observed, a recent study showed that nearly one third of doctors stated that they would automatically suspend a patient's DNR order during anesthesia.[7] The most pervasive argument advanced in favor of the unsolicited suspension of DNR orders during anesthesia is that the

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chance of survival after an arrest in the operating room (OR) is higher than elsewhere (without quantifying the alleged survival).[8] This assumption is based on the studies showing that the outcomes of witnessed in-hospital cardiac arrests are better than those of unwitnessed arrests, especially when the cause is iatrogenic.[9,10] For out-of-hospital cardiac arrest, the American Heart Association relies on a survival rate between 2 and 11% globally[11,12] and less than 15% in the United States.[11,13–15]

The presupposition is that the altered circumstances of the OR lead to better prognoses: In the OR, cardiac arrests are always witnessed, and trained staff is present to deliver CPR immediately. If so, surgical patients with DNR orders should be provided the information relevant for deciding how they want anesthesiologists to manage their DNR orders during general anesthesia. To provide an evidence base for ethical management of DNR orders for the general population during anesthesia and surgery, we performed a systematic review of the literature in this area to quantify the survival (within the studied time periods) after any given attempt at intraoperative CPR.

Materials and Methods

This study was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[16]

Search Strategy and Selection

A systematic search was performed in the PubMed, EMBASE, and Scopus literature databases on August 22, 2014, for records published between 1990 and August 2014 using synonyms for intraoperative and CPR or cardiac arrest (appendix). Two independent assessors (S.K. and J.M.) screened the titles and abstracts of the retrieved records for inclusion, and duplicates were excluded using predefined eligibility criteria. Publications consisting of original studies reporting on outcomes defined as mortality and/or morbidity of perioperative CPR in patients undergoing elective surgery were included. The scope of the research question was extended to the perioperative setting as arrests occurring in the immediate postoperative period are always witnessed and can be still considered either surgery or anesthesia related. Because the surgical procedures that the patients with DNR orders undergo are predominantly nonemergent (ranging from palliative surgery to life-extending interventions),[17] publications regarding emergency and trauma surgery were excluded. Studies exclusively investigating pediatric patients or perioperative cardiac arrests related to otherwise specific conditions or procedures (such as congenital heart disease and liver transplantation surgery) were excluded from further review because they were not considered representative for the target population. Case studies, animal studies, and publications written in languages other than English and Dutch were not included for further review. Subsequent full-text screening of the included articles by two independent assessors resulted in a more confined selection for final analysis. All studies that concerned CPR other than manual CPR were additionally excluded. In addition, reference lists of the selected studies were checked for articles missed in the initial search.

Study Assessment

This review aims to assess the survival rate after intraoperative CPR among the general surgical population because resuscitation in patients with DNR orders is a semantic impossibility, and thus, systematic analysis of survival among our target population is lacking. However, to provide some insight into survival among this subgroup, study samples were evaluated based on the inclusion of elderly patients and/or patients with considerable comorbidities undergoing solely elective surgery. Because all publications retrieved by the search are in essence outcome predictor studies rather than prevalence studies, risk of bias was assessed in terms of a clear definition of the CPR technique used and the percentage of missing data. High risk of bias was assessed when a description of the used CPR technique was lacking and more than or equal to 10% of the data was missing.

Data Extraction

The following data were extracted from the included articles by two independent reviewers (S.K. and J.M.): year of publication, number of cardiac arrests (and subsequent CPR attempts), age, ASA physical status classification, type of surgical procedure, place where the cardiac arrest occurred, outcome, and study methods. The primary outcome measure was overall survival within the studied time period(s). The secondary outcome measure was quality survival, defined as functional outcome or morbidity otherwise specified, within the studied time period(s). When mortality rates were given, survival rate was calculated. Preferably, overall survival and quality survival were given as the percentage of the total number of studied intraoperative or perioperative cardiac arrests.

Results

Search Strategy and Selection

The database search yielded a total of 363 unique records after deduplication (fig. 1). Thirteen studies remained after selection based on title and abstract. Subsequent full-text screening resulted in exclusion of another six studies (see fig. 1 for reasons) leading to the inclusion of seven studies (table 1). Cross-reference checking revealed that additional articles were not missed by the initial search.

Study Assessment

All but one study provided a clear description of the CPR technique applied and reported less than 10% missing data, rendering overall internal validity of the studies high (table 2). Results from the study by Constant *et al.*[19] express comparatively lower validity because the lack of (described) standardized CPR and missing data could have biased results. However, applicability of patient samples to the target population overall is limited. Only one study[18] included patients with two of three DNR-like characteristics (elderly

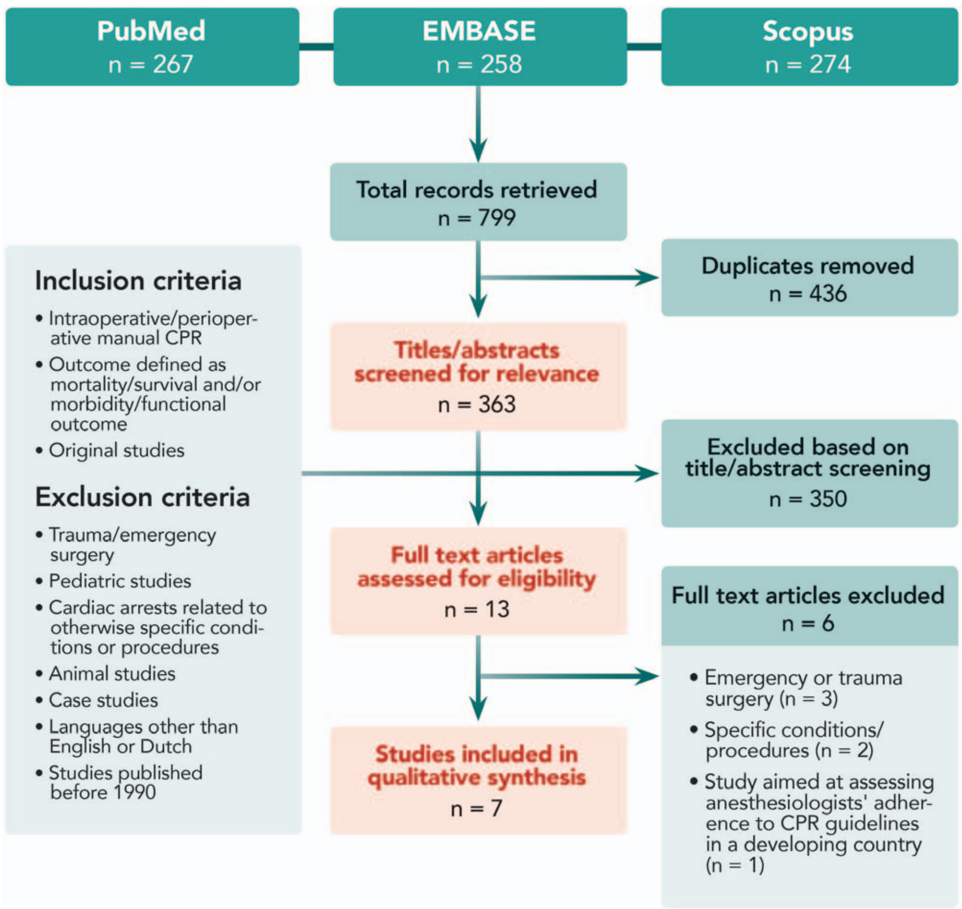

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram of the selection and inclusion of publications. CPR = cardiopulmonary resuscitation.

Table 1. Study Characteristics

			Patients			Setting	Intervention	Outcome
Study	Sample Size	Study Design	Age (yr)	Physical Status	Type of Procedure	Place Where Arrest Occurred	CPR	Survival within 24 h (%)
Nunes *et al.*[18]	100	P	≥60	Majority ASA III–V	None excluded	OR/PACU	Yes	32.0
Constant *et al.*[19]	140	R	≥18	NR	None excluded	OR/PACU	Yes	32.0
Ramachandran *et al.*[20]	2,524	P	≥18	NR	None excluded	OR/within 24 h postoperatively	Yes	45.5
Goswami *et al.*[21]	262	P	≥16	Majority ASA III–V	No trauma and cardiac surgery	OR/PACU	Yes	55.7
Braz *et al.*[22]	186	P	No age limit	Majority ASA III–V	None excluded	OR/PACU	Yes	36.6
Braz *et al.*[23]	138	P	No age limit	Majority ASA III–V	None excluded	OR/PACU	Yes	35.5
Sprung *et al.*[24]	223	R	No age limit	NR	No cardiac procedures	OR/PACU	Yes	46.6

Sample size = number of cardiac arrests (and subsequent CPR attempts); physical status = American Society of Anesthesiologists physical status; Outcome = survival within 24 h after CPR.

ASA = American Society of Anesthesiologists; CPR = cardiopulmonary resuscitation; NR = data not reported; OR = operating room; P = prospective; PACU = postanesthesia care unit; R = retrospective.

Table 2. Assessment of Methodologic Quality and Applicability of Included Studies

	Applicability			Internal Validity	
Study	Elderly Patients	Severe/Comorbid Diseases	Only Elective Procedures	CPR Clearly Defined	<10% Missing Data
Nunes *et al.*[18]	■	■	□	■	■
Constant *et al.*[19]	□	?	□	□	□
Ramachandran *et al.*[20]	□	?	□	■	■
Goswami *et al.*[21]	□	■	□	■	■
Braz *et al.*[22]	□	■	□	■	■
Braz *et al.*[23]	□	■	□	■	■
Sprung *et al.*[24]	□	?	□	■	■

■ = yes; □ = no; ? = unclear, no information provided.

Table 3. Overall Survival and Quality Survival after Perioperative CPR

Ranking	Study	Survival within 24 h (%)	Survival at Hospital Discharge	30-d Survival	90-d Survival	Quality survival (CPC 1) at Hospital Discharge	90-d Quality Survival (CPC 1 or 2)
1	Nunes *et al.*[18]	32.0	NA	NA	NA	NA	NA
2	Constant *et al.*[19]	32.0	NA	NA	30.3%	NA	45.3%
3	Ramachandran *et al.*[20]	45.5	31.7%	NA	NA	64.0%	NA
4	Goswami *et al.*[21]	55.7	NA	37.4%	NA	NA	NA
5	Braz *et al.*[22]	36.6	NA	NA	NA	NA	NA
6	Braz *et al.*[23]	35.5	NA	NA	NA	66.8%*	NA
7	Sprung *et al.*[24]	46.6	34.5%	NA	NA	NA	NA

* Patients in regular general status after anesthesia-related cardiac arrest, not measured in CPC scores.
CPC score = Cerebral Performance Category score; CPR = cardiopulmonary resuscitation; NA = not available; 1 = no major disability; 2 = moderate disability.

patients and/or patients with considerable comorbidities undergoing solely elective surgery), whereas the remaining six samples[19–24] only displayed one characteristic.

Data Extraction

Overall Survival. Overall survival rates ranged from 32.0 to 55.7% when measured within the first 24 h after perioperative CPR, across seven heterogeneous patient samples.[18–24] The lower end of this range encompasses the findings from a study among elderly patients with considerable comorbidities, whereas the higher end consists of findings from studies investigating intraoperative CPR during noncardiac surgery. A slight decrease in survival rate was observed over time in all studies that measured survival after the first 24 h: survival rate decreased to 31.7% (from 45.5% survival ≤24 h) and 34.5% (from 46.6% survival ≤24 h)[20,24] at hospital discharge, and at 30 and 90 days postoperatively survival rate decreased to 37.4% (from 55.7% survival ≤24 h) and 30.3% (32.0% crude intensive care unit [ICU] survival), respectively.[19,21]

Constant *et al.*[19] analyzed 140 adult patients who were admitted to the ICU after successful intraoperative resuscitation. Of these patients, 76 of 140 patients (54.3%) survived their stay at the ICU. During the 90-day follow-up, one patient was lost to follow-up after hospital discharge and four other patients died, yielding an overall survival of 72 of 140 (51.4%) patients after initially successful intraoperative CPR. However, of all 238 resuscitated patients, 98 were excluded because of death occurring in the OR (initial survival 58.8%). This results in an overall survival of 76 of 238 (32.0%) patients at ICU discharge and 72 of 238 (30.3%) patients at 90 days follow-up after intraoperative CPR (table 3). Ramachandran *et al.*[20] found that 1,151 of 2,524 (45.5%) patients survived 24 h after their cardiac arrest (58% occurring in the OR and 42% in the postanesthesia care unit [PACU] within 24 h after surgery) and 799 of 2,524 (31.7%) patients survived to hospital discharge. Nunes *et al.*[18] demonstrated that 32 of 100 (32.0%) patients older than 60 yr experiencing intraoperative (93% OR and 7% PACU) cardiac arrest survived. Two previous studies by the same study group examined perioperative cardiac arrests in all age groups at the same hospital during a cumulative timeframe.[22,23] Therefore, it is likely that some of the cardiac arrests in the study by Nunes *et al.* were also included in these two previous studies. The first of these studies demonstrated 49 of 138 (35.5%) survivors after perioperative (93% OR and 7% PACU) resuscitation.[23] The consecutive study at the same center observed survival of 68 of 186 (36.6%) patients receiving perioperative (95% OR and 5% PACU) resuscitation.[22] Sprung *et al.*[24] found that 104 of 223 (46.6%) patients experiencing cardiac arrest during their time in the OR until recovery discharge or ICU transfer survived at least 1 h and also found that 77 of 223 (34.5%) patients survived to hospital discharge. Goswami *et al.*[21] prospectively analyzed intraoperative cardiac arrest in patients undergoing noncardiac surgery and found that 146 of 262 (55.2%) patients survived at 24 h and 98 of 262 (37.4%) patients survived at 30 days.

Quality Survival. A favorable neurologic outcome was observed in 64.0 to 66.8% of studied survivors at hospital discharge[20,23] and in 45.3% of survivors at 90 days follow-up.[19] Three studies reported on quality survival after perioperative CPR in the general surgical population. Constant *et al.*[19] showed that 63 of 139 (45.3%) patients who were admitted to the ICU after successful CPR after intraoperative cardiac arrest (intraoperative period was defined as the time spent in the OR) had a favorable 90-day functional outcome. Favorable outcome was defined as Cerebral Performance Category (CPC) score 1 or 2, that is, "alive with good cerebral performance or sufficient cerebral function for independent activities of daily life, with or without mild neurological or psychologic deficits."[19] Ramachandran *et al.*[20] showed that 473 of 739 (64.0%) survivors of perioperative (OR, PACU, or within 24 h after PACU discharge) cardiac arrest with valid CPC scores had a CPC score of 1 at hospital discharge. The authors also showed that among patients with normal baseline neurologic status, although the number of comorbidities was associated with worse survival to discharge and worse survival at 24 h, comorbid disease burden bore no apparent relationship with neurologic outcome among those surviving to hospital discharge. Braz *et al.*[23] found that 31 of 49 (63.3%) patients surviving perioperative CPR were in poor general status, 26.7% in regular general status, and 10% in good general status at PACU discharge. With respect to hospital discharge conditions of patients with anesthesia-related cardiac arrests, the authors showed that 36.4% were in poor general status and 66.8% were in regular general status.

Discussion

In this study, we aimed to quantify survival after intraoperative CPR among the general surgical population to aid ethical management of DNR orders during general anesthesia. Survival measured within the first 24 h after perioperative CPR was 32.0 to 55.7%,[18–24] with survival among elderly patients at the lower end of the range. These figures decreased slightly when survival was measured at hospital discharge (31.7 to 34.5%).[20,24] Two studies included longer follow-up time in which a decrease in survival was observed from 55.7% within the first 24 h to 37.4%[21] 30 days postoperatively and from 32.0% crude ICU survival to 30.3% 90 days postoperatively.[19] We retrieved only three publications from our systematic literature search that reported on functional outcomes after perioperative CPR (quality survival). Of studied survivors, 45.3 to 66.8% experienced a favorable neurologic outcome,[19,20,23] meaning that these patients were able to live independent lives, with or without mild neurologic impairments. These figures suggest that viable survival after perioperative CPR can be roughly estimated at 25% (approximately 50% survival with 50% good recovery in survivors). One study showed that the risk of patient harm (facilitating survival, but with new neurologic deficits) did not increase among patients with normal baseline neurologic status, even when they suffered from considerable comorbidities.[20]

The majority of previous publications on intraoperative cardiac arrest have reported on incidence and overall survival as a means to explore ways to improve anesthesia care. Thus, the studies included in this review all consist of outcome predictor studies. However, our objective is to enable patients with DNR orders to modify their treatment limiting directives for the course of a surgical procedure by communicating the range of (quality) survival after perioperative CPR. Because the lower limit of the range for survival within 24 h is 32% after perioperative CPR and the average survival after CPR in other settings is less than 15%,[11] it seems that among the general surgical population, the probability of surviving perioperative CPR is higher than in other settings. We note that patients with DNR orders generally display characteristics that negatively affect the outcome of CPR in other settings, such as multiple comorbidities and high age. Therefore, the study by Nunes *et al.*[18] seems to be most reflective of the surgical population with DNR orders (survival ≤24 h 32.0%). Conversely, only patients undergoing elective surgery will be in the position to modify their DNR orders preoperatively. Our results show that when trauma surgery and cardiac procedures are excluded, survival seems better (46.6 to 55.7%).[21,24]

Our findings are supported by a recent study by Nunnally *et al.*[25] showing an immediate survival after perioperative cardiac arrest of 41.6% (n = 1,691,472). These data suggest that perioperative factors and the immediate availability of skilled anesthesia care influence survival outcomes of CPR. Thus, the foreseeable outcome after resuscitation in the OR appears better compared with the outcome that the patient would have had in mind when filling out the initial DNR order (based on <15% survival of out-of-hospital cardiac arrest). We acknowledge that our results are not fully generalizable to patients with DNR orders undergoing general anesthesia, and survival rates may in fact be worse for patients with severe co-existing disease (as a result of which a DNR order has been put in place). However, we stress that survival among the general surgical population is the best proxy at hand to assess the probability of successful intraoperative CPR for patients with DNR orders. First, these data provide relevant empirical input for the ASA's requirement for preoperative reconsideration of treatment limiting directives and, second, demonstrate that survival rates in the OR are not as favorable as one might expect. These insights may reduce the level of moral distress that anesthesiologists can experience when certain patients decide to retain their DNR orders, thus increasing willingness to routinely implement preoperative conversations for reassessing treatment limiting directives during general anesthesia.

We recommend a preoperative conversation in which the anesthesiologist and the patient (or the designated surrogate) can come to consensus about whether to resuscitate and if so, to what extent. Through shared decision-making, consensus may be established to fully suspend the DNR order or to opt for a "limited" attempt at resuscitation in which the patient (or designated) surrogate can choose to continue to refuse certain specific resuscitation procedures (*e.g.*, defibrillation or tracheal intubation) that would reasonably lead to aggressive or intensive care treatment. In some cases, all parties may concede to retain the DNR order under general anesthesia; however, attempts should be made to understand why the patient wishes the surgery but does not wish the procedures that are essential to the success of the anesthesia and the surgery. Some patients express the fear of becoming dependent on others or living in a vegetative state after surviving a cardiac arrest, whereas others may hold the view that an attempt of resuscitation interferes with what they consider a dignified way of dying. Exposing fears and goals should guide discussions about modifying treatment limiting directives.

As such, discussing the different options would mean that patients who have a DNR order that includes refraining from intubation have the opportunity to opt for intubation and mechanical ventilation on a temporary basis when they experience respiratory arrest during general anesthesia for a palliative procedure. Conversely, exsanguinating hemorrhage from an unexpected gastrointestinal bleed in a patient with end-stage Alzheimer disease might well not be treated with aggressive transfusion per patient and family wishes. Herein, the causal factors requiring any intervention that falls under the term "resuscitation" are relevant as well as the context of the situation and the patient's stated goals.

Our review had a number of limitations. Only one study looked strictly at the time a patient spent in the OR to assess the incidence of cardiac arrest,[19] whereas other studies included a more extended monitored period (PACU or ICU). Ramachandran *et al.*[20] included cardiac arrests occurring at any location within 24 h after surgery, without recording whether the wards patients were admitted to provided monitoring. Because cardiac arrests detected by monitoring are found to be four times more likely to result in return of spontaneous circulation after CPR than those detected by pulse palpitation, it can very well be that the figures by Ramachandran *et al.* underestimated survival and functional outcome. Also, five of seven studies were single-center studies,[18,19,22–24] thus their findings may not be representative of survival in other hospitals. Results from three separate publications reported the proceedings of research done over a cumulative time period within the same prospective database of a particular university hospital in Brazil.[18,22,23] Not only will the patients included overlap to a certain degree but the teaching hospital is also located in a developing country limiting generalizability as a correlation between developing countries and higher incidences of cardiac arrest with higher mortality has been reported.[26] With respect to the synthesis of the publication findings, we stress that our results may not be generalizable to environments outside the OR where anesthesia is required and a DNR order is in place. Thus, future work is recommended on assessing survival after cardiac arrest during anesthetic procedures outside the traditional OR environment.

Given the fact that as many as 15% of the patients with DNR orders receive surgery (mostly as a part of palliative care to improve their level of comfort),[27] ethical management of treatment limiting directives is of significant and increasing concern in the OR environment. Qualitative research underlines patients' wishes for a preoperative discussion to determine how their DNR orders should be respected during the perioperative period.[28] The ASA's guidelines have already emphasized the importance of respecting patient autonomy by requiring a conversation between doctors and patients with DNR orders to discuss these issues preoperatively.[6] Decisions about the management of DNR orders in the light of procedures that require anesthesia are substantially complex decisions and should center around expected clinical outcome, causal factors, clinical judgment, and the patient's stated goals and fears.

An overall survival rate between 32.0 and 55.7% and a favorable neurologic outcome between 45.3 to 66.8% may be valued differently by different people, both patients and doctors, and thus can aid the type of shared decision-making required in these conversations and relieve doctors from moral distress when certain patients decide to retain their DNR orders.

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Competing Interests

The authors declare no competing interests.

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Appendix. Search strategy (Date of Search: August 22, 2014)

Database	Search
PubMed	(((((((((intraoperative cardiac arrest*[Title/Abstract]) OR intraoperative cardiopulmonary arrest*[Title/Abstract]) OR perioperative cardiac arrest*[Title/Abstract]) OR perioperative cardiopulmonary arrest*[Title/Abstract]) OR anesthesia-related cardiac arrest*[Title/Abstract]) OR anesthesia related cardiac arrest*[Title/Abstract]) OR anesthesia-related cardiopulmonary arrest*[Title/Abstract]) OR anesthesia related cardiopulmonary arrest*[Title/Abstract]) OR intraoperative resuscitation[Title/Abstract]) OR perioperative resuscitation[Title/Abstract]) OR intraoperative cardiopulmonary resuscitation[Title/Abstract]
EMBASE	(intraoperative cardiac arrest*: ti,ab or intraoperative cardiopulmonary arrest*: ti,ab or perioperative cardiac arrest*: ti,ab or perioperative cardiopulmonary arrest*: ti,ab or perioperative cardiac arrest*: ti,ab or perioperative cardiopulmonary arrest*: ti,ab or anesthesia-related cardiac arrest*: ti,ab or anesthesia related cardiac arrest*: ti,ab or anesthesia-related cardiopulmonary arrest*: ti,ab or anesthesia related cardiopulmonary arrest*: ti,ab or intraoperative resuscitation: ti,ab or perioperative resuscitation: ti,ab)
Scopus	(TITLE-ABS-KEY("intraoperative cardiac arrest*" OR "intraoperative cardiopulmonary arrest*" OR "perioperative cardiac arrest*" OR "perioperative cardiopulmonary arrest*") OR TITLE-ABS-KEY("anesthesia-related cardiac arrest*" OR "anesthesia related cardiac arrest*" OR "anesthesia-related cardiopulmonary arrest*" OR "anesthesia related cardiopulmonary arrest*") OR TITLE-ABS-KEY("intraoperative resuscitation" OR "perioperative resuscitation" OR "intraoperative cardiopulmonary resuscitation"))