Effect of dopexamine infusion on mortality following major surgery: Individual patient data meta-regression analysis of published clinical trials

Rupert M. Pearse, FRCA, MD; Jonathan D. Belsey; Julian N. Cole, MRCPI; E. David Bennett, FRCP

Objectives: **To establish whether perioperative low-dose dopexamine infusion (≤1 μg/kg/min) is associated with a reduction in mortality and duration of hospital stay following major surgery.**

Data Source: **MEDLINE, EMBASE, CINAHL, Cochrane Library, Google Scholar, and reference lists.**

Study Selection: **Two reviewers independently screened studies for inclusion, assessed trial quality, and extracted data. Eligible trials were randomized controlled trials comparing dopexamine infusion to control treatment. Data are reported as odds ratios (ORs) or hazard ratios (HRs) with 95% confidence intervals.**

Data Extraction: **Systematic review and meta-regression analysis of individual patient data.**

Data Synthesis: **Five studies fulfilled the inclusion criteria. Analysis of pooled data from high- and low-dose dopexamine groups identified a reduction in duration of hospital stay (median 14 vs. 15 days; HR 0.85 [0.73–0.91]; $p = .03$) but no improvement in mortality (9.1% vs. 12.3%; OR 0.78 [0.31–1.99]; $p = .61$). However, low-dose dopexamine was associated with a 50% reduction in 28-day mortality (6.3% vs. 12.3%; OR 0.50 [0.28–0.88]; $p = .016$) as well as a reduced duration of stay (median 13 vs. 15 days; HR 0.75 [0.64–0.88]; $p = .0005$). When high-dose dopexamine groups were compared with controls, there was no difference in either mortality (OR 1.06 [0.60–1.87]; $p = .85$) or duration of stay (HR 1.04 [0.94–1.16]; $p = .36$).**

Conclusions: **For pooled data describing perioperative dopexamine infusion at all doses, there was an improvement in duration of hospital stay but no survival benefit. However, at low doses, dopexamine was associated with improved survival and reduced duration of stay. Further clinical trials are warranted to confirm this observation. (Crit Care Med 2008; 36:1323–1329)**

KEY WORDS: dopexamine; surgery; mortality; oxygen delivery; perioperative care

Perioperative care of the high-risk patient is an important but neglected area of clinical practice. Recently, a large U.K. study identified a high-risk population of surgical patients that accounted for 13% of inpatient general surgical procedures but >80% of postoperative deaths (1). Data from North America support the existence of a significant high-risk surgical population and suggest that the long-term survival of those patients who develop postoperative complications but survive to leave the hospital is also drastically reduced (2). These data confirm the need for improved standards of perioperative care for the high-risk surgical patient.

The association between cardiovascular derangements and outcome following high-risk surgery is well described (3–7). These observations have led to the use of fluid and inotropic therapy to increase cardiac output and systemic oxygen delivery during the perioperative period and thus improve outcome (8–13). One of the most frequently used agents for this purpose is the dopamine analogue dopexamine (9–13), which possesses agonist activity at β_2 and dopaminergic (DA_1 and DA_2) receptors but no intrinsic action at α-adrenergic receptors (14). Potential beneficial mechanisms of this agent may include enhanced tissue perfusion and anti-inflammatory effects (15, 16).

However, the findings of perioperative trials of dopexamine have proved inconsistent. In some studies, dopexamine use was associated with reduced morbidity or mortality (9, 12, 13); in others, there was no difference from conventional treatment (10, 11). One explanation for these findings may be the wide variation in the dose of dopexamine used. Anecdotal evidence suggests that most clinicians now use dopexamine at doses $<1\ \mu g \cdot kg^{-1} \cdot min^{-1}$. This probably relates to an increased incidence of tachycardia associated with higher doses, which could increase myocardial oxygen demand, thus negating other beneficial effects. The aim of this study was to examine individual patient data from published clinical trials to establish whether the perioperative infusion of dopexamine at doses $\leq 1\ \mu g \cdot kg^{-1} \cdot min^{-1}$ is associated with reductions in mortality and duration of hospital stay using a meta-regression approach. In contrast to conventional random effects meta-analysis, this method allows the impact of treatment allocation to be clearly distinguished

From the Royal London Hospital, Whitechapel, London, United Kingdom (RMP); JB Medical Ltd, Little Cornard, United Kingdom (JDB); Roche Products Limited, Welwyn Garden City, United Kingdom (JNC); and St George's Healthcare NHS Trust, London, United Kingdom (EDB).

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For information regarding this article, E-mail: rupert.pearse@bartsandthelondon.nhs.uk

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from patient factors, in particular baseline characteristics.

MATERIALS AND METHODS

Literature Search

Searches of the MEDLINE, EMBASE, CINAHL, and Cochrane Central databases up to July 2006 were carried out by two authors using the following search terms: (dopexamine OR dopacard) AND (surgery OR surgical OR *operative OR operation) AND (randomized OR randomised). No restrictions were placed on language or source. A further online search was then carried out using the Google Scholar search engine, using the following key words: dopexamine, surgery, randomized, randomised. Bibliographies of reports of randomized trials and relevant reviews were also screened. Based on the frequency of publications identified in this search, a manual search of editions of *Acta Anaesthesiologica Scandinavica*, *Anaesthesia and Intensive Care*, *British Journal of Anaesthesia*, *Critical Care*, *Critical Care Medicine*, *Intensive Care Medicine*, and the *European Journal of Anaesthesiology* from the previous 20 yrs was also performed.

Selection

The resulting abstracts were screened to identify randomized controlled trials comparing dopexamine infusion with a control group in patients undergoing major abdominal, vascular, or urologic surgery. Studies were excluded if mortality and length of stay were not reported or if the studies had not been published in a peer-reviewed journal. Where the abstracts indicated that a study was likely to fulfill these criteria, the full text was obtained.

Validity Assessment

All studies that met the inclusion criteria were quality appraised to maximize inter- and intraobserver consistency using a previously validated scoring system (17). Each study was assessed according to a 5-point scale, with 1 point being awarded for each of the following criteria: randomized trial, details of randomization method provided, double-blinded trial, details of blinding method provided, information on study withdrawals provided. Studies failing to score $\geq$3 points were excluded from the analysis.

Data Extraction and Study Characteristics

Once qualifying studies had been identified, the authors and sponsors were contacted and asked to supply individual patient data regarding age, treatment, duration of postoperative stay, and mortality. Two meta-regression analyses were performed to allow quantification of the effect of dose and other study-related differences on 28-day mortality and duration of hospital stay. In some trials, the study protocol required the use of a fixed dose of dopexamine (10, 11), whereas in others the dose of dopexamine was selected according to cardiac output and oxygen delivery measurements (9, 12, 13). Some patients allocated to the dopexamine treatment group of these studies may not have received dopexamine if oxygen delivery spontaneously achieved the predetermined goal. To account for this potential source of bias, two analyses were performed: an intention-to-treat analysis, in which patients were categorized according to their potential to have received dopexamine in a treatment group indicated in the protocol, and a per-protocol analysis, where patients were allocated to groups on an individual basis according to whether they had actually received dopexamine.

Quantitative Data Synthesis

Mortality rates were examined as a binary outcome with a multilevel logistic regression approach using study group, age, dopexamine dose, and volume of intravenous fluid (crystalloid and colloid combined) as potential explanatory variables. Based on the maximum dopexamine infusion rate given within each randomized group, patients were placed in one of three categories: control, low-dose dopexamine (≤ 1 $\mu g \cdot kg^{-1} \cdot min^{-1}$), and high-dose dopexamine (>1 $\mu g \cdot kg^{-1} \cdot min^{-1}$). The probability of death was allowed to vary across studies, in an approach analogous to traditional random effects meta-analysis. Estimation was performed using a first-level marginal quasi-likelihood model, the results of which informed a second-level predictive quasi-likelihood estimation. Odds ratios (ORs) were calculated for both dopexamine treatment groups vs. control, tested for significance against the normal distribution, and are reported with 95% confidence intervals (CIs). Statistical significance of between-variable interactions was estimated using the Wald test.

The dates of surgery and hospital discharge were ascertained to allow the calculation of postoperative duration of stay for patients who did not die in the first 28 days. This was analyzed as a survival function, and a Cox proportional hazards model used to estimate hazard ratios (HRs) for each dopexamine dose category vs. control. The model was stratified by study to allow for between-center survival differences. Z values for between-treatment differences in hazard ratios were tested against the normal distribution. Analyses were performed using MLwiN version 2.01 and EpiInfo version 3.3.2.

RESULTS

Study Characteristics

The initial search identified 51 titles. After initial screening by abstract, five qualifying studies were identified (Table 1 and Fig. 1) (9–13). These involved 483 patients allocated to dopexamine groups and 350 patients allocated to control groups. Individual patient data were available from all of the studies and were carried forward for the meta-analysis. The median age was 68 yrs (range 18–91), 540 patients were male (65%), and 102 patients underwent surgery on an emergency basis (12.2%).

Qualitative Data Synthesis

Intention-to-Treat Analysis of Pooled Data From High- and Low-Dose Dopexamine Groups. Eighty-seven patients died in the first 28 days postoperatively, 43 in the control group (12.3%) and 44 in the dopexamine groups (9.1%) (Table 2). Patients were allocated to receive an adrenaline infusion in a third treatment arm of one study, the results of which have not been included (13). Treatment group and patient age were both identified as independent predictors of mortality risk in the two-level predictive quasi-likelihood regression model (Supplementary Table 1, available online). Although volume of fluid administered was identified as a significant independent predictor of mortality, this did not differ significantly between treatment groups: median (interquartile range) volumes of intravenous fluid administered were as follows: control group 3000 mL (1800–4800); low-dose dopexamine group 3200 mL (2400–4900); high-dose dopexamine group 3700 mL (2040–6500). Neither gender nor urgency of surgery (as defined by the original study investigators) exerted an independent effect on mortality (Table 2). Once age, treatment group, and fluid volume were taken into account, there were no significant residual between-studies or between-centers effects (chi-square 0.387, $p = .53$; and 1.232, $p = .27$, respectively). Based on these models, adjusted ORs were calculated for each dose group. There was no significant difference in 28-day mortality risk among patients randomized to treatment with dopexamine vs. patients allocated to control treatment (OR 0.78 [CI 0.31–1.99]; $p = .60$).

Table 1. Eligible studies identified in the systematic review.

Reference	Patient Type	Dopexamine Dose in Intervention Group(s)	Number of Patients (ITT Analysis)		Age (Median SD)		Non-Elective Surgery (%)		28-Day Mortality (%)		Median Duration of Stay (Days)	
			Dopex	Control	Dopex	Control	Dopex	Control	Dopex	Control	Dopex	Control
Boyd et al (13)	Major general, vascular and urological surgery	≤1.0 $\mu g \cdot kg^{-1} \cdot min^{-1}$	27	54	67 (10.6)	72 (12.0)	9 (35%)	17 (31%)	0	22.2	12	13
		>1.0 $\mu g \cdot kg^{-1} \cdot min^{-1}$	26		69 (12.8)		12 (44%)		15.4		14	
Wilson et al (9)	Major general, vascular and urological surgery	Starting dose 0.125 $\mu g \cdot kg^{-1} \cdot min^{-1}$	46	46	70 (5.0)	72 (7.0)	0 (0%)	0 (0%)	4.3	13.0	10	13
Takala et al (10)	Major abdominal surgery	0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$	135	140	61 (14.5)	63 (13.5)	11 (8.1%)	21 (15%)	7.4	12.9	15	17
		2.0 $\mu g \cdot kg^{-1} \cdot min^{-1}$	137		64 (12.2)		18 (13.1%)		14.6		17	
Stone et al (11)	Major abdominal surgery	0.25 $\mu g \cdot kg^{-1} \cdot min^{-1}$	50	50	70 (7.0)	69 (6.0)	0 (0%)	0 (0%)	4.0	2.0	13	13
Pearse et al (12)	Major general, vascular and urological surgery	Starting dose where indicated in protocol 0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$	62	60	68 (11.6)	66 (11.4)	7 (12%)	6 (10%)	9.7	11.7	11	14

ITT; Intention to treat, Dopex; dopexamine

Duration of hospital stay data were available for 746 patients who did not die within 28 days of surgery (control group 307 patients, low-dose dopexamine group 320 patients, high-dose dopexamine group 119 patients). Duration of stay ranged from 2 to 213 days (median 14 days [CI 10–24]). Log (duration of stay) was approximately normally distributed and yielded a geometric mean of 16.3 days. Survival functions were constructed using a Cox proportional hazards model, with study center, age, gender, intervention group, volume of intravenous fluid received, and urgency of surgery acting as potential predictor variables (Supplementary Table 2, available online). In the pooled dopexamine dose model, age, gender, and study center were not found to exert an effect on duration of hospital stay and were excluded from the final model. Treatment with dopexamine at any dose was found to be associated with a significantly shorter duration of stay than control treatment (HR 0.85 [CI 0.73–0.91]; $p = .03$).

Intention-to-Treat Analysis of the Effects of Low- and High-Dose Dopexamine. Of the 44 deaths in the dopexamine groups, 20 occurred in the low-dose group (6.3%) and 24 in the high-dose group (14.5%) (Table 2). In two studies, patients received either low- or high-dose dopexamine on an intention-to-treat basis and were allocated to these groups accordingly (10, 13). These crude aggregated results yielded an odds ratio of 0.54 for low-dose dopexamine vs. control and 1.37 for high-dose dopexamine vs. control. Primary 3 × 2 chi-square testing confirmed that the overall difference across groups was statistically significant (chi-square 8.28; $p = .016$). Based on the two-level regression model (Supplementary Table 1), adjusted odds ratios were calculated, taking into account differences in age, gender, center, fluid volume, and urgency of procedure. Patients treated with low-dose dopexamine were significantly less likely to die within 28 days of surgery than those allocated to control groups (OR 0.50 [CI 0.29–0.88]; $p = .016$). However, no significant difference in mortality between the high-dose dopexamine and control groups was identified (OR 1.06 [CI 0.60–1.87]; $p = .85$) (Fig. 2 and Table 2). The Cox regression analysis was repeated using the dose subgroupings for dopexamine (Supplementary Table 3, available online). Low-dose dopexamine infusion was associated with a significant reduction in duration of stay (HR 0.75 [CI 0.64–0.88]; $p = .0005$). No significant difference in duration of stay was identified between the high-dose dopexamine and control groups (HR 1.04 [CI 0.94–1.16]; $p = .36$) (Table 3).

A subgroup analysis of patients undergoing elective and nonelective surgery was also performed with corrections for age, gender, volume of intravenous fluid administered, and stratified by study center. Some 724 patients underwent elective surgery, of whom 301 were allocated to control groups with 30 deaths (10.0%), 285 received low-dose dopexamine with 18 deaths (6.3%) (adjusted OR vs. control = 0.64 [0.21–1.94]; $p = .43$), and 138 received high-dose dopexamine with 21 deaths (15.2%) (adjusted OR vs. control = 1.09 [0.36–3.29]; $p = .87$). Some 109 patients underwent nonelective surgery, of whom 49 were allocated to control groups with 13 deaths (26.5%), 33 received low-dose dopexamine with two deaths (6.1%) (adjusted OR vs. control = 0.14 [0.01–1.82]; $p = .14$), and 27 received high-dose dopexamine with three deaths (11.1%) (adjusted OR vs. control = 0.51 [0.06–4.18]; $p = .53$).

Per-Protocol Analysis of the Effects of Low- and High-Dose Dopexamine. For the purposes of the per-protocol analysis, 24 patients were reallocated to different treatment groups, of whom three died within 28 days. Twenty-three patients who were allocated to low-dose dopexamine groups in the original studies but did

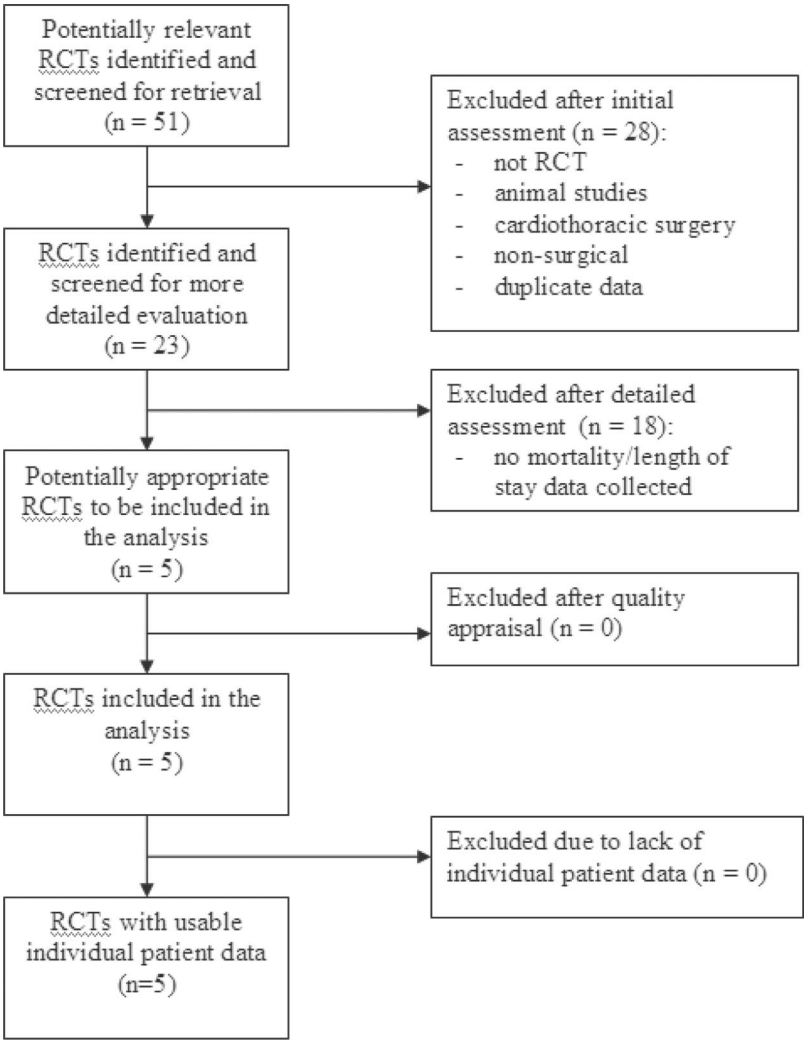

Figure 1. Flowchart illustrating reasons for study rejection or inclusion in the analysis. *RCT*, randomized controlled trial.

Table 2. 28-day mortality for low-dose dopexamine, high-dose dopexamine, pooled dopexamine and control groups as determined by intention-to-treat and per-protocol analyses.

	28-Day Mortality		
Treatment Group	n/N (%)	OR (95% CI)	*P* vs Control
Intention-to-treat analysis			
Control	43/350 (12.3%)	1.0	—
Dopexamine (all doses)	44/483 (9.1%)	0.78 (0.31–1.99)	0.61
Low-dose dopexamine	20/320 (6.3%)	0.50 (0.28–0.88)	0.016
High-dose dopexamine	24/163 (14.7%)	1.06 (0.60–1.87)	0.85
Per-protocol analysis			
Control	46/372 (12.4%)	1.0	—
Low-dose dopexamine	17/296 (5.7%)	0.46 (0.25–0.83)	0.0099
High-dose dopexamine	24/165 (14.5%)	1.06 (0.60–1.86)	0.85

OR, odds ratio; CI, 95% confidence intervals

not actually receive dopexamine were reallocated to the control group. Two patients who were allocated to low-dose dopexamine groups in the original studies received dopexamine at a dose >1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and were reallocated to the high-dose dopexamine group. One patient allocated to a control group received low-dose dopexamine in violation of the protocol and was reallocated to the low-dose dopexamine group. Consequently, in this analysis, there were 46 deaths in the control group (12.4%), 17 in the low-dose dopexamine group (5.7%), and 24 in the high-dose dopexamine group (14.5%) (Table 2). These crude aggregated results yielded a risk ratio of 0.43 for low-dose dopexamine vs. control and 1.21 for high-dose dopexamine vs. control. Primary 3×2 chi-square testing confirmed that the overall difference across groups was highly statistically significant (chi-square 9.41; $p = .009$). Once again, both two-level regression models identified treatment group, patient age, and fluid volume administered as independent predictors of mortality (online supplementary tables). In the per-protocol analysis, median (interquartile range) volumes of intravenous fluid administered were as follows: control groups 3000 mL (1750–4500); low-dose dopexamine group median 3500 mL (2500–5000); high-dose dopexamine group 3700 mL (2040–6500). Gender and urgency of surgery exerted no significant independent effect, and there were no significant between-studies or between-centers effects once age, treatment group, and fluids were taken into account (chi-square 0.669, $p = 0.41$; and 1.084, $p = .30$, respectively).

The findings of the per-protocol analysis were very similar to those of the intention-to-treat analysis. The use of low-dose dopexamine was associated with a significant reduction in mortality even after patients who spontaneously attained a predefined goal for systemic oxygen delivery were reallocated from the low-dose dopexamine to the control group (OR 0.46 [CI 0.25–0.83]; $p = .0099$). Similarly, there was no difference in mortality between the high-dose dopexamine and control groups (OR 1.06 [CI 0.60–1.86]; $p = .85$) (Fig. 3 and Table 2). In the per-protocol analysis of duration of hospital stay, the results were once again similar to those of the intention-to-treat analysis with a significant reduction in duration of stay associated with low-dose dopexamine compared with the control group (HR 0.76 [CI 0.64–0.89]; $p = .001$) (Table 3). There was no difference in duration of stay between the high-dose dopexamine and control groups (HR 1.05 [CI 0.95–1.17]; $p = .32$).

DISCUSSION

The principal finding of this analysis was that perioperative dopexamine infusion affects outcome in a dose-dependent manner. The analysis of pooled data from

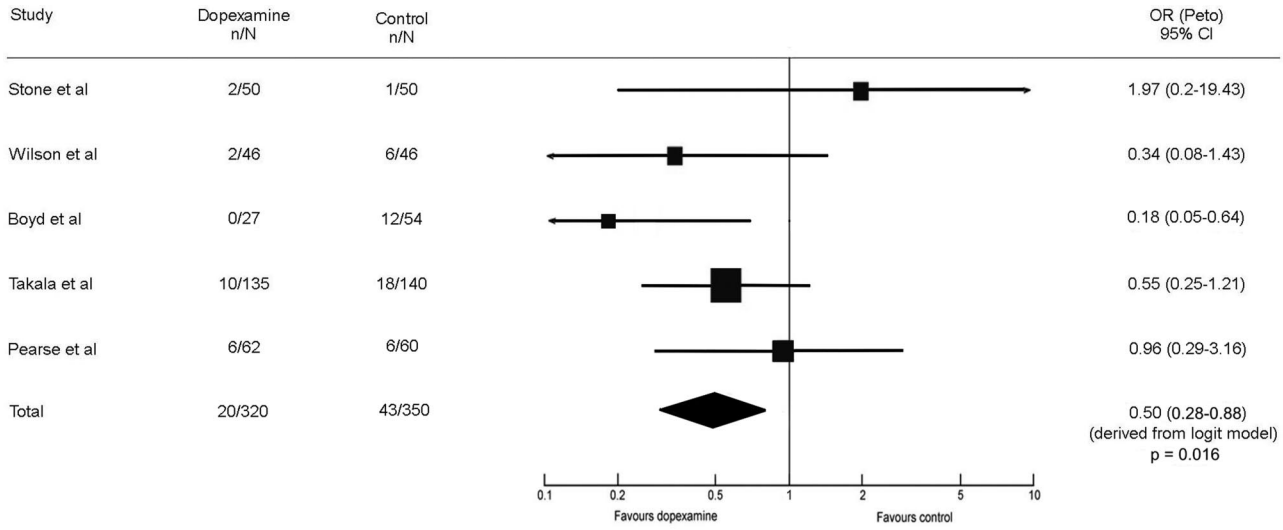

Figure 2. Twenty-eight-day mortality for low-dose dopexamine groups compared with control groups for intention-to-treat analysis (does not include data on patients allocated to high-dose dopexamine group). *OR*, odds ratio; *CI*, confidence interval.

Table 3. Duration of hospital stay for low-dose dopexamine, high-dose dopexamine, pooled dopexamine and control groups as determined by intention-to-treat and per-protocol analyses.

Treatment Group	Duration of Stay (Days)		HR vs Control (95% CI)
	Mean (SD)	Median (IQR)	
Intention-to-treat analysis			
Control	23.5 (22.8)	15 (11–27)	—
Dopexamine (all doses)	20.7 (21.9)	14 (10–22)	0.85 (0.73–0.91)
Low-dose dopexamine	18.1 (17.4)	13 (9–20)	0.75 (0.64–0.88)
High-dose dopexamine	26.1 (28.6)	17 (10–29)	1.04 (0.94–1.16)
Per-protocol analysis			
Control	23.1 (22.6)	15 (11–27)	—
Low-dose dopexamine	18.2 (17.3)	13 (9–20)	0.76 (0.64–0.89)
High-dose dopexamine	26.1 (28.6)	17 (10–29)	1.05 (0.95–1.17)

HR; hazard ratio, SD; standard deviation, IQR; inter-quartile range

high- and low-dose dopexamine groups failed to identify any survival benefit, although there was a reduction in duration of postoperative stay among survivors. However, low-dose dopexamine infusion (≤ 1 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was associated with a considerable survival benefit in addition to a greater reduction in duration of hospital stay. In contrast, at doses >1 $\mu g \cdot kg^{-1} \cdot min^{-1}$, dopexamine was not associated with any improvement in either mortality or duration of hospital stay. Taking previous mortality estimates for patients undergoing major surgery into account (1), these findings suggest that the use of low-dose dopexamine could prevent $>10{,}000$ perioperative deaths each year in the United Kingdom alone. The reductions in duration of hospital stay are likely to reflect reductions in postoperative complication rates and also suggest that the use of low-dose dopexamine infusion may be associated with significant cost savings. Economic analysis of two of the trials selected in this analysis suggests this is the case even where the perioperative use of dopexamine necessitates admission to a critical care unit (18, 19).

Only one of the component studies identified a significant improvement in survival associated with dopexamine (13). The remaining trials, which included a multicenter trial (10), did not identify a survival benefit of dopexamine at either low or high doses. This will be explained, at least in part, by the fact that each of the component trials lacked statistical power for a survival outcome. However, it remains a possibility that our findings arose as a result of heterogeneity within and between trials. Of particular relevance in this analysis were differences in urgency of surgery, trial centers, and treatment protocols. Comparison of the summary results of the component studies does indicate significant heterogeneity. However, we have taken a number of measures to account for this. The use of individual patient data in a multilevel regression model allowed us to control for differences between patients, studies, and treatment centers within studies. This approach is more robust than conventional meta-analysis, which may still allow uncontrolled differences to obscure true results. Once dose, age, volume of intravenous fluid use, and urgency of surgery had been taken into account, no significant between-studies or between-centers differences were demonstrated for mortality and there was only a small residual effect for duration of stay that was independent of the benefit of low-dose dopexamine. In each of the component studies, the confidence intervals for mortality, and duration of hospital stay were consistent with the central estimate derived from the meta-analyses. Another important factor was that in three of the studies, dopexamine was not administered at a fixed dose but commenced only in patients who failed to achieve a predefined goal for systemic oxygen delivery (9, 12, 13). Once commenced, the dose was increased on an incremental basis until this target was achieved. In some cases, this target was achieved spontaneously and consequently a number of patients allocated to intervention groups did not receive dopexamine. A good postoperative outcome would be more likely for such patients (3–7). We therefore performed an additional per-protocol analysis in which patients were allocated to control, low-dose dopexamine, and high-

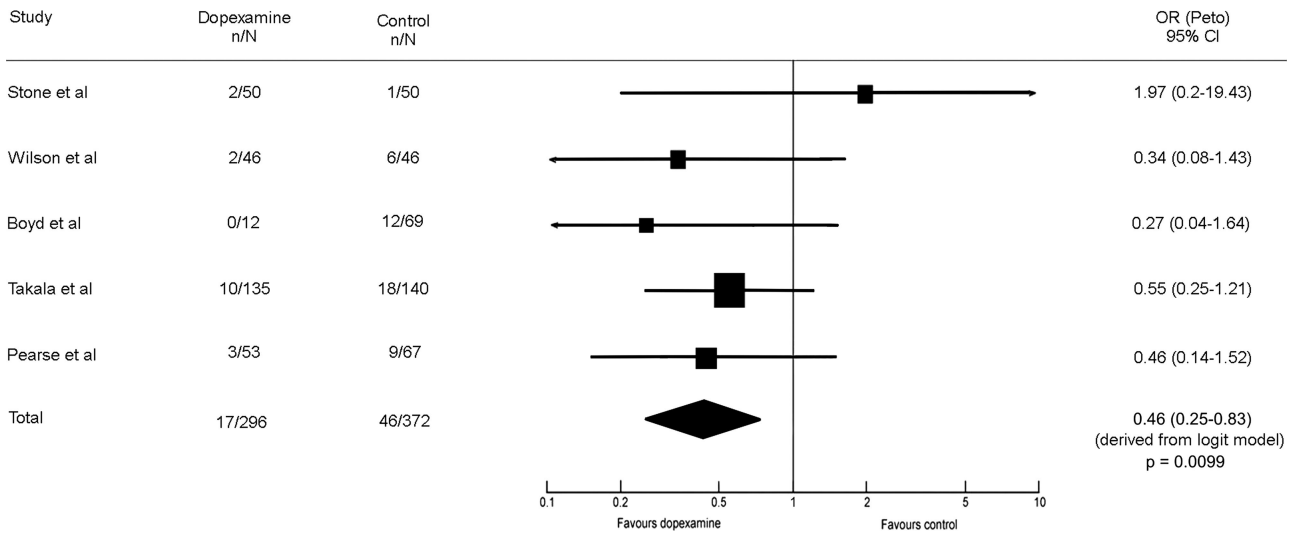

Figure 3. Per-protocol analysis of 28-day mortality for patients who received low-dose dopexamine compared with control patients who did not receive dopexamine (does not include data on patients allocated to high-dose dopexamine group). *OR*, odds ratio; *CI*, confidence interval.

dose dopexamine groups according to the dose of dopexamine received. The reallocation of 24 patients from their original intention-to-treat groups in the per-protocol analysis did not significantly alter the findings. While there was an association between mortality and the volume of intravenous fluid administered, this was similar in the different groups and did not influence the association between low-dose dopexamine use and survival. This is not entirely surprising given the inconsistent findings of trials investigating restrictive vs. liberal perioperative fluid regimes (20, 21). The findings of the subgroup analyses for patients undergoing elective and nonelective surgery were also consistent with the overall findings of this study. While none of these results were statistically significant, this is likely to relate to the reduced sample sizes. It may have been preferable to allocate patients to study groups based on the total dose of dopexamine received, but these data were not available. Each of the five randomized controlled trials of perioperative dopexamine use identified in the literature search was included in this analysis. All the authors and/or sponsors granted full access to the available data, and we are not aware of any unpublished trials that would have been eligible for inclusion.

Dopexamine is believed to improve outcome through enhanced oxygen delivery to the tissues, although the precise mechanism of benefit has not been fully elucidated. There is some evidence to suggest that dopexamine may enhance microvascular perfusion (15), although a specific effect on splanchnic and renal vascular beds remains unconfirmed (22). Alternatively, the observed improvements in outcome may relate to effects on capillary permeability or inflammatory pathways (16, 23). The apparent dose-related effects of dopexamine may relate to an unidentified inverse dose-response effect or to a changing spectrum of receptor activity. However, it seems most likely that the beneficial effects of dopexamine are negated by side effects at higher doses. In the largest study, high-dose dopexamine was associated with tachycardia in $\geq$55% of patients (10). It is quite possible that the resulting increase in myocardial oxygen demand could negate any beneficial effects. While the postoperative use of low-dose dopexamine is also associated with increases in heart rate, this does not appear to affect the incidence of myocardial injury as determined either by electrocardiographic criteria or cardiac troponin assays (24).

CONCLUSIONS

In high-risk patients undergoing major surgery, dopexamine infusion at doses of $\leq 1\ \mu g \cdot kg^{-1} \cdot min^{-1}$ was associated with reductions in 28-day mortality and duration of hospital stay in survivors. The analysis of pooled data from high- and low-dose dopexamine groups failed to identify any survival benefit, although there was a small reduction in duration of stay. At higher doses, the beneficial effects of dopexamine appear to be negated by side effects, in particular tachycardia. Further, adequately powered, clinical trials are warranted to confirm the efficacy of low-dose dopexamine in patients undergoing major surgery.

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