Meta-Analysis

Adverse heart rate responses during beach-chair position for shoulder surgeries - A systematic review and meta-analysis of their incidence, interpretations and associations

Address for correspondence:
Dr. Thrivikrama Padur Tantry, Department of Anaesthesiology, A J Institute of Medical Sciences, Kuntikana - 575 004, Mangalore, Karnataka, India.
E-mail: drpttantry@yahoo.com

Submitted: 10-Mar-2020
Revised: 02-May-2020
Accepted: 07-Jul-2020
Published: 31-Jul-2020

Access this article online

Website: www.ijaweb.org

DOI: 10.4103/ija.IJA_228_20

Quick response code

Thrivikrama Padur Tantry, Harish Karanth, Reshma Koteshwar, Pramal K Shetty, Karunakara K Adappa, Sunil P Shenoy[1], Dinesh Kadam[2], Sudarshan Bhandary[3]

Departments of Anaesthesiology, [1]Urology, [2]Plastic and Reconstructive Surgery and [3]Orthopedics, Arthroscopy and Sports Medicine, A J Institute of Medical Sciences and Research Centre, Kuntikana, Mangalore, Karnataka, India

ABSTRACT

Background and Aims: Evaluations of adverse heart rate (HR)-responses and HR-variations during anaesthesia in beach-chair-position (BCP) for shoulder surgeries have not been done earlier. We analysed the incidence, associations, and interpretations of adverse HR-responses in this clinical setting. **Methods:** We performed a meta-analysis of trials that reported HR-related data in anaesthetised subjects undergoing elective shoulder surgeries in BCP. Studies included prospective, randomised, quasi-randomised and non-randomised, controlled clinical trials as well as observational cohorts. Literature search was conducted in MEDLINE, EMBASE, CINHAL and the Cochrane Central Register of Controlled Trials of the 21st century. In the first analysis, we studied the incidence and associations of bradycardia/hypotension-bradycardia episodes (HBE) with respect to the type of anaesthesia and different pharmacological agents. In the second, we evaluated anaesthetic influences, associations and inter-relationships between monitored parameters with respect to HR-behaviours. **Results:** Among the trials designed with bradycardia/HBE as a primary end point, the observed incidence of bradycardia was 9.1% and that of HBE, 14.9% and 22.7% [(for Interscalene block (ISB) ± sedation) subjects and general anaesthesia (GA) + ISB, respectively]. There was evidence of higher observed risk of developing adverse HR-responses for GA subjects over ISB (Risk Difference, $P < 0.05$). Concomitant use of β-agonists did not increase risk of HBEs ($P = 0.29$, $I^2 = 11.4\%$) or with fentanyl ($P = 0.45$, $I^2 = 0\%$) for ISB subjects (subgroup analysis). Fentanyl significantly influenced the HR-drop over time [meta-regression, estimates (standard error), 14.9 (5.4), 9.8 (4.3) and 17 (2.6); $P = 0.007$, 0.024 and <0.001; for early, mid and delayed periods, respectively] in GA subjects. With respect to number of subjects experiencing cerebral desaturation events (CDEs), total intravenous anaesthesia (TIVA)- propofol had higher risk over inhalational anaesthesia ($P = 0.006$, $I^2 = 86.7\%$). Meta-correlation analysis showed relationships between the HR and rSO_2 (regional cerebral oxygen saturation) or $SjvO_2$ (jugular venous oxygen saturation) values ($r = 0.608$, 95%CI, 0.439 to 0.735, $P < 0.001$, $I^2 = 77.4\%$ and $r = 0.397$, 95%CI, 0.151 to 0.597, $P < 0.001$, $I^2 = 64.3\%$, respectively). **Conclusions:** There is not enough evidence

How to cite this article: Tantry TP, Karanth H, Koteshwar R, Shetty PK, Adappa KK, Shenoy SP, *et al*. Adverse heart rate responses during beach-chair position for shoulder surgeries - A systematic review and meta-analysis of their incidence, interpretations and associations. Indian J Anaesth 2020;64:653-67.

to claim the associations of adverse HR-responses with any specific factor. HR-fall is maximal with fentanyl and its variability is associated with changes in rSO_2. Fall in rSO_2 could be the common link triggering adverse HR-responses in BCP.

Level and Quality of Evidence: Level of evidence, IIA/IIB; GRADE recommendation, B.

Key words: Adrenergic beta-receptor agonists, arthroscopy, bradycardia, fentanyl, oximetry, shoulder, sitting position

INTRODUCTION

Among the undesirable haemodynamic consequences of beach-chair position (BCP) for shoulder (arthroscopic) surgeries, bradycardia, by virtue of its unpredictable occurrence and occasionally adverse anaesthetic consequences, is a cause for concern.[1-4] A specifically named haemodynamic event, the 'Hypotension-Bradycardia Episode' (HBE) has been reported in 6-27% of BCP subjects.[3-5] These studies however lack specificity in documenting isolated significant bradycardia (necessitating the use of atropine). The true incidence of bradycardia remains indeterminate due to several factors such as the frequent use of the terms 'bradycardia' and 'HBEs' as synonyms,[4,6] use of different definitions of 'bradycardia' by various authors, inclusion of additional causes of 'hypotension' episodes (anaesthetic and pharmacological) and subjective variations in the anaesthesiologist's decision to use atropine, justifiably attributable to a 'play it safe' attitude.

The correlation of incidence of bradycardia/HBE with the type of anaesthesia[5] or the anaesthetic agent deployed has not been conclusively established.[7] While activation of the Bezold-Jarish Reflex (BJR) linked to interscalene block of the brachial plexus (ISB) could be the primary reason for such adverse events,[8] the demonstration of a 'non-empty' heart ventricle during such events suggests otherwise.[9-11] Similarly, the association of use of β-adrenergic agonists and adverse heart rate (HR)-responses/HBE[2,4] is uncertain since these episodes were also reported in patients without their use.[12,13] Likewise, while ISB has been linked to such events,[8] the same has not been confirmed with general anaesthesia (GA). There is a paucity of comparative literature on the association of HR-responses in BCP with other parameters like use of maintenance anaesthetic agents or opioids. Several studies indicate a strong association of hypotensive response with regional cerebral oxygen saturation (rSO_2)[14-16] and jugular venous oxygen saturation ($SjvO_2$) for BCP surgeries done under anaesthesia.[16] But it is unclear whether cerebral desaturation events (CDEs) correlate with (adverse) HR-responses.

The aim of this study was to systematically review all available evidence from trials reporting bradycardia/HBEs for its: 1) incidence, 2) anaesthetic/pharmacological associations, and 3) association of BCP-HR-behaviours with monitored parameters, and to conduct a meta-analysis on the results. Establishing the association of adverse haemodynamic responses with specific anaesthesia-related variables or changes in monitored parameters would be helpful in improving predictability of such events, taking precautionary measures to prevent them and providing an insight into their possible underlying pathophysiological mechanisms.

METHODS

Registration and protocol

This meta-analysis was conducted in accordance with Preferred Reporting Items for Systematic reviews and Meta-analyses.[17] The protocol was registered with PROSPERO (CRD42019119454, crd.york.ac.uk; date of registration, 14/01/2019, and updated on 31/07/2019).

Eligibility criteria

We included prospective, randomised, quasi-randomised and non-randomised, controlled clinical trials as well as observational cohorts with adult subjects (>18 yrs) undergoing elective shoulder surgeries in BCP. Reporting of HR-related data or HR-responses were mandatory to inclusion. Publications in all languages were considered. Subjects received one of the following anaesthetic modalities; (1) Planned GA; (2) Regional anaesthesia (RA): ISB or similar and (3) RA in combination with GA. The use of supplementary sedation was not a barrier to inclusion. We excluded studies wherein subjects underwent

surgeries in <45° BCP as well as American Society of Anaesthesiologists (ASA) >3 physical status.

Information sources

An electronic literature search was conducted in MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials and CINHAL. The selection of literature specifically restricted to studies in BCP. We also searched the bibliography of retrieved manuscripts for additional studies pertaining to data encompassing our primary outcome of interest. These comprised studies reporting incidents of isolated bradycardia or HBEs, documenting maximum and minimum average HRs, or measuring serial HR over time periods; with a caveat that both pre-induction and post-induction HR data be available. Twenty-first-century literature were scanned since anaesthesia protocols have remained uniform during this period. Retrospective studies, reviews with inadequate information on primary outcome interests, abstracts and letters to the editor were not included. The detailed search strategy is shown in Supplementary Digital Content File 1.

Study selection and data collection

The manuscripts meeting the inclusion criteria were assessed and data were extracted following a standardised format. Extracted items comprised of study characteristics, risk of bias (RoB) domains,[18] participant disposition, and study outcomes. *Patients* were categorised according to type of the surgery or anaesthesia, number of subjects and position adopted for surgery (≥45° of BCP, i.e., 45 to 90°). *Interventions* referred to BCP after induction and achievement of hemodynamic stability. *Comparison* of variables was pre-BCP versus post-BCP. *Outcomes* were classified as 'primary' and 'secondary'. The former included HR data before and after BCP at various intervals of time, the incidence of bradycardia/HBE in BCP, influence of anaesthetics over HR-responses and HR-rSO_2/$SjvO_2$ associations. The latter included incidence and magnitude of hypotension and associations of mean blood pressure (MBP) with anaesthetic factors, vasoactive drugs and rSO_2/$SjvO_2$ in BCP.

Data synthesis and analysis of outcomes

For evaluation of the outcome of interests of this interventional (investigating an effect of BCP on HR) meta-analysis, data were extracted separately from study groups (SGs) of each trial to negate the effect of intergroup variables affecting their outcomes. We categorised the SGs further into study control groups, randomised SGs, non-randomised SGs, physiological control groups. Study control groups received standard anaesthesia care without additional investigating pharmacological agents or technical measures. Physiological control groups were those placed in BCP but not anaesthetised.

The HR data collected included values documented at a single point of time or continuous data at various intervals for a SG. Incidences of bradycardia and/or HBE and rest of the HR data were considered for meta-analysis. Data were collected as a single or combined value in the form of mean and standard deviations (SD) or median and inter-quartile range (IQR), respectively. If multiple data were provided, then they were converted into pooled statistical averages. The data were tabulated under pre-induction [baseline (BL)] and post-induction groups. The latter included data relating to pre-BCP and post-BCP categories after the stabilisation of vitals. These post-BCP HR data were pooled for the time periods mentioned in the respective publication. If recorded data timings were non-specific timings, they were approximated to a specific time by mutual discussion with the two authors. Publications with unreported or inconclusive data that could not be obtained after attempts to contact the authors were excluded from this review.

The data presented in tables, text or images were used as the primary source for extraction. A graph digitizing software (Enguage Digitizer version 10.10, @ Mark Mitchell) was used for efficiently extracting and estimation of numerical raw data whenever text numerical data were unavailable. We substituted the missing SDs with pooled SDs of other studies with the same comparison by $\sqrt{[(\sum N^{*}SD^{2})/\sum N]}$ where N = sample size. When range and IQR were available, SD was estimated using the formula SD = range/4 and SD = IQR/1.35, respectively, as described by Cochrane Hand Book of Systematic Reviews.[19] Data were reported as 95% confidence intervals (CI). The median was used to estimate the mean if the value was not reported. Whenever standard error of mean (SEM) was reported, SD was obtained as $SD = SEM\sqrt{N}$. If data were provided as % of change over a BL numerical value, they were converted to numbers. To account for drop out cases over time or termination of BCP before the time specified in the meta-analysis, subject numbers were approximated to the nearest values for pooled data estimation. If the exact time point was not specified in the manuscript, then the approximated time point was considered by the authors' judgment.

We used individual definitions for defining events of bradycardia, HBE, hypotension and CDEs as described by authors of each study. Dichotomous data like bradycardia, hypotension, CDEs, etc. were converted into incidence (*n*/N) for a given time interval. The single highest incidence was used to capture the proportion of subjects who experienced a certain adverse response at least once. Data from SGs receiving more than one intervention or different anaesthetic agent or a technique (within a SG) were combined into a single group as per Cochrane Hand Book.[19] Data were clubbed together into a single group whenever the primary authors grouped the study subjects on the basis of an event. Finally, 'intention to treat' basis was used for analysing complications-related data in some SGs. Subjects were repositioned back to supine following BCP-induced haemodynamic disturbances.[20]

Data synthesis specific to HR

Incidence of bradycardia/HBE was considered whenever the events were reported either individually or synonymously in the subject at least once. To differentiate isolated bradycardia from the broader term, HBE, we considered the use of atropine (*n*/N) for defining the former. Data relating to HR-variability over time were again sub-divided into immediate/early (~10 minutes, EHR), mid (11-30 minutes, MHR) and delayed (after 30 minutes till the end of BCP, DHR). The magnitude of changes over time was represented by mean differences (MDs).

Data synthesis specific to blood pressures (BPs)

MBP was considered for data evaluation and the data synthesis was similar to that followed for HR. We excluded pooled data of systolic or diastolic blood pressures. Whenever SDs were not reported for nadir values, they were imputed from pooled SDs of the same group. All analysis was done presuming no incidence of hypotension in the supine position under anaesthesia. Subjects who were excluded prior to surgery, after BCP, owing to severe hypotension were also included (intention to treat).

Data synthesis specific to CDEs

For analysing CDEs, two types of rSO_2 values (MDs) were considered; (1) MDs of pre and post-BCP (pooled), as 'absolute' values; (2) MDs of pre-BCP and 'lowest' achieved post-BCP rSO_2 values. Lowermost of lowest was considered whenever right and left cerebral hemispheres were recorded separately (with single or two different methods). Whenever SDs were not reported for nadir rSO_2 values, they were imputed from pooled SDs of the same group. All analysis was done presuming no incidences of CDEs in supine position under anaesthesia.

Pre-defined sources of heterogeneity

To explore the potential causes of heterogeneity in our results that could influence primary outcome results, we pre-identified certain clinical aspects of individual SGs. These included (1) randomisation technique; (2) anaesthetic technique; (3) induction agent; (4) maintenance anaesthetic agent; (5) use of opioids; (6) use of vasoactive agents. Equivalent doses of ephedrine and phenylephrine were considered for vasopressor consumption, converting ephedrine doses to their phenylephrine equivalence using a potency ratio of 81.2: 1.[21]

The degree to which some of these additional factors predict EHRs, MHRs and DHRs was evaluated using a meta-regression analysis. To examine the influence of different anaesthetic agents, opioids, vasoactive drugs or eligibility criteria on HR-variability, we performed a sensitivity analysis. Sub-group analysis was considered based on: (1) type of anaesthesia; (2) predisposing or preventing agent; or (3) the maintenance agent for both incidences of bradycardia/HBE and serial HR measurements. Additional analyses ('leave-one-out' analysis, correlation statistics and meta-correlation analysis) were considered as necessary (for primary outcomes).

Meta-analysis was conducted with Review Manager (RevMan) 5.3 (Cochrane Collaboration, Copenhagen, Denmark, 2014). The random effects model was used for all analyses. Heterogeneity was measured and expressed as I^2.[22] Meta-regression was performed using JASP software (Version 0.9.2, BibTeX, Amsterdam).[23] This analysis excluded subjects administered with ISB ± sedation since the anaesthetic agent influences on HR are largely absent. Meta-regression (Restricted-Maximum-Likelihood method, random effects) was performed for EHR with priori defined factors, induction agents, opioids and use of PVIs. For MHR and DHR, maintenance anaesthetic agents and opioids were considered.

For continuous variables (HR, absolute and lowest achieved cerebral saturations), MDs were compared using the inverse-variance (I-V) method. For dichotomous variables (incidences of bradycardia, HBEs, CDEs, hypotension), odds ratio (OR), risk

ratio (RR) or risk differences (RD) were computed by the Mantel-Haenszel (M-H) or I-V methods. Natural log-transformation was adopted[24] as the outcomes for incidences were expected to be non-normal. Publication bias was checked using regression test for funnel plot asymmetry and Egger's test (JASP software, version 0.9.2).[25] Correlations were attempted for those SGs which mentioned statistical averages of consecutive measurements of HR, rSO_2 and $SjvO_2$ on the one hand and for MBP and rSO_2 on the other. Meta-correlation analysis was performed after obtaining a series of correlation coefficients for various SGs using MedCalc® Version 14.8.1, MedCalc Software bvba, 2014. For all, statistical significance was set at $P < 0.05$ (2-tailed).

RESULTS

Summary of results for various outcomes are provided in Table 1.

Literature identification

From 2306 studies that were initially screened, 661 potentially relevant manuscripts were selected based on the abstract. The details pertaining to literature identification are provided in the flow chart (Supplementary Digital Content File 2). Finally, 47 trials provided the data for analysis (from year 2000 to 2019).

Study characteristics

We included all SGs of manuscripts that provided HR data. Hence, the majority of manuscripts had two or more SGs. Supplementary Digital Content File 3 summarises the characteristics of SGs including Jadad scores. In total, there were 91 SGs for this review (n = 3107), 70 SGs detailed about serial HR measurements, additional to the adverse HR-responses. There were 67 randomised SGs (RCTs, n = 29). Supplementary Digital Content File 4 depicts the RoB graph and summary. Thirty-nine SGs were considered as study control groups and four as physiological study controls. One trial (year 1998)[26] was included against the PRISMA protocol, as the same was used by the rest of the authors to define HBE.

First analysis

Bradycardia and/or HBE

Bradycardia/HBE was reported in 24 SGs.[4,6,12,13,26-32] For defining 'bradycardia/HBE', primary authors used their own criteria for 8 SGs. The rest followed the definition by Liguori *et al*.[26] The incidence of isolated bradycardia[12,13,27-30] varied from 0 to19% (n = 65 of 712, 9.1%) and that of HBE,[4,6,12,13,26,28-32] 5 to 28% (n = 147 of 988, 14.9% in ISB subjects and n = 255 of 1121, 22.7% in ISB and GA subjects).

Meta-analysis of the incidence of bradycardia revealed risk ratio of 9.8 [(RR, 95%CI; 4.4, 21.9), I^2 = 0%, $P < 0.0001$] and HBE, RR of 19.6 [(95%CI; 10.7, 35.8), $I^2 = 0\%$, $P < 0.00001$] in BCP. There was evidence of higher observed 'excessive risk' of developing adverse responses for GA subjects over ISB (RD $P < 0.05$, Figure 1).

Primary authors proposed the possible associations of adverse HR-responses with various factors (epinephrine, fentanyl, ISB, norepinephrine, ondansetron or β-adrenergic blockers). Very low evidence was observed to confirm their effects on adverse HR-responses in ISB subjects. However, further analysis revealed that the use of β- adrenergic agonists[4,6,26,32] and fentanyl[12,13,28] did not increase risk of HBEs without its use [test for sub-group difference, P = 0.29, I^2 = 11.4% and P = 0.45, I^2 = 0%, respectively (Figure 2)]. Effect of prophylactic ondansetron (4-8 mg) in prevention of HBE was analysed in 2 trials;[13,28] meta-analysis revealed OR (non-event, 95%CI) of 4.13 (1.89, 9.02, $P = 0.0004$). Effect of prophylactic use of β-blocker was used in one study[26]; meta-analysis revealed OR (non-event, 95%CI) of 5.8 [1.65, 20.36, $P = 0.006$ (Figure 3)]. In 17 SGs, the timing of bradycardia/HBE was documented. Pooled data showed the timing of occurrence as 33.6 ± 24 minutes.[4,6,12,13,26,28,31] All BCP surgery subjects received midazolam, fentanyl or propofol sedation alone or in combination in ISB group at different doses and timings.

Second analysis

Post-BCP HR-responses analysed from serial HR measurements [Figure 4]

Our meta-analysis of HR-responses over time considered two sub-groups based on the type of anaesthesia and maintenance agents used. BL-HR was reported in 48 SGs (n = 1334); 12 used TIVA-propofol[16,33-37] (73.7 ± 13.4 beats/min, n = 451), 33 received inhaled anaesthetics[16,29,35,38-50] (73.6 ± 13.6 beats/min, n = 744) and 139 subjects had ISB.[6,50] MDs between HR-values at supine (Pre-BCP) and post-BCP status are depicted in Figure 4.

Sensitivity analysis revealed that various anaesthetic agents significantly influenced fall in HRs. However, it made little difference to the overall results when

Table 1: Summary of results

Parameter analysis	*n*	Outcome	Comments (GRADE recommendation)
Definition of bradycardia/HBE	1121	Definition of bradycardia/HBE varied much between authors; therefore, the diversified incidence reporting.	Majority of authors used definition by Liguori *et al*.[a]
Incidence of bradycardia and anaesthetic influences	712	9.1% of subjects are reported with bradycardia with RR of 9.8, after positioning to BCP. ISB had no excessive risk of developing bradycardia over GA.	Limited data available for GA subjects (⊕⊕⊕○-moderate, for overall and all subgroups)[f]
Incidence of HBE and anaesthetic influences	1121	15% of ISB and 23% of GA+ISB subjects are reported with HBE with odds of 30, after positioning to BCP. It appears that GA was associated with higher (excessive) risk over ISB.	Limited data available for GA subjects; since anaesthetic causes of hypotension incidences are simultaneously included, may over-estimate the true incidences. (⊕⊕○○-low, ⊕○○○-very low, ⊕⊕⊕○-moderate; for overall, ISB±sedation, GA±ISB subgroups.)[f]
Timing of bradycardia/HBE	848	Varied significantly in literature; 70% of study groups report the mean timing of adverse HR responses occurring after 30 minutes. Pooled data average timings are 33.6±24 minutes	SDs are high for the pooled data
Effect of β-agonists (epinephrine) on bradycardia/HBE incidences	988	No evidence of excessive risk of developing HBEs with use of β-agonists compared to subjects without its use.	Epinephrine was used either during ISB local anaesthetic block placement or for saline irrigation fluid of arthroscopy (⊕⊕○○-low; for overall or subgroups analysis)[f]
Effect of fentanyl on bradycardia/ HBE incidences	775	No evidence of excessive risk of developing HBEs with use of fentanyl compared to subjects who did not receive it.	Only the studies which have used fentanyl in every subject, were included for analysis (⊕⊕○○-low, ⊕⊕⊕⊕-high, ⊕⊕⊕○-moderate; for overall, and for subgroup analysis, respectively)
Effect of prophylactic ondansetron and β-blockers on bradycardia/HBE incidences	395	Evidence of lower risk of developing HBE with the use; ondansetron may decrease the incidence by 4 times	Limited number of trials available for β-blocker prophylaxis (⊕⊕⊕○-moderate; for both outcomes)[f]
Serial HR measurements and effect of type of anaesthesia	1453, 1315, 802[b]	Administering GA or GA+ISB is associated with progressive fall of HR over time and this is maximum after 30 minutes under anaesthesia at BCP. Addition of ISB did not cause additional fall in HR.	Pooled measurements were considered
Serial HR measurements and effect of maintenance anaesthetic agent	1363, 1163, 580[c]	Subjects with TIVA-propofol and ISB subjects had least fall of HR, over time, in BCP.	Pooled measurements were considered
Serial HR measurements and effect of intraoperative pharmacological agent	Variable	Evidence of highest fall of HR with the use of fentanyl alone (for mid and delayed HR) or for concomitant use of fentanyl and PVIs (for early) is observed.	Limited data is available for fentanyl-PVIs concomitant effects.
Incidence of hypotension and type of anaesthesia (number of subjects)	2366	Evidence of higher 'excessive' risk for number of subjects who developed hypotension at BCP for subjects administered with GA over GA+ISB or ISB±sedation.	Incidences of 'HBE' were considered for ISB subjects
Incidence of hypotension and maintenance anaesthetic agent (number of subjects)	1251	Use of TIVA-propofol was not associated with excessive risk of developing hypotension over inhaled anaesthetics	Few of the TIVA-propofol group subjects had concomitant use of PVIs at the beginning of BCP
CDEs and maintenance anaesthetics	684	Maintenance anaesthetics can influence the CDEs; TIVA-propofol was associated with higher 'excessive' risks for number of subjects who experienced CDEs than inhalational agents.	
CDEs and ISB anaesthesia	30	Shoulder surgeries done under ISB alone was associated with least incidences of CDEs.	Only one SG of this meta-analysis has been considered for CDE evaluation.
rSO_2 and maintenance agents (absolute fall)	849	Absolute fall of rSO_2 was not influenced by different maintenance anaesthetics; however, a non-statistically significant higher desaturation values were recorded for TIVA-propofol compared to inhaled anaesthesia subjects.	The immediate corrective therapy during a rSO_2 fall may not reflect the actual differences

Contd...

Table 1: Summary results

Parameter analysis	*n*	Outcome	Comments (GRADE recommendation)
rSO_2 and maintenance agents (lowest achieved)	599	Lowest achieved rSO_2 was not influenced by different maintenance agents. However, a non-statistically significant higher desaturation values were recorded for TIVA-propofol compared to inhaled anaesthesia subjects.	The immediate corrective therapy during a rSO_2 fall may not reflect the actual differences
rSO_2 - HR relationships	381	Meta-correlations reveal that HR measurements from serial recordings of several study groups statistically correlated well with the respective rSO_2 measurements	Statistical correlations were derived from consecutive, serial measurements.
$SjvO_2$ - HR relationships	186	Meta-correlations reveal that HR measurements from serial recordings of few study groups statistically correlated well with respective $SjvO_2$ values	Statistical correlations were derived from consecutive measurements but the strength of correlation was weak.
Influence of PVIs on HR	165	PVIs did not influence HR fall with in study subjects; however, the magnitude of HR fall was higher compared to control subjects.	Limited data available
Influence of PVIs on HR -rSO_2/ $SjvO_2$ relationships	90	PVIs have not influenced the CDEs and HR-rSO_2/$SjvO_2$ relationships.	Limited data available
rSO_2 - MBP relationships	457	Meta-correlation analysis revealed a statistically significant correlation between MBP and rSO_2 values	Predictable outcome
Vasopressor consumption[d]	503	Pooled averages of ephedrine requirements were higher for GA±ISB than GA alone to maintain the desired BP.	Limited data and non-parametric data comparisons.
HR of physiological matched controls	199[e]	HR increased or remained same in subjects after positioning to BCP.	Physiological controls are those who did not receive any pharmacological agents.

BCP – Beach chair position; BP - Blood pressure; CDE – Cerebral desaturation event; GA – General anaesthesia; GRADE – Grading of Recommendations Assesment, Development and Evaluation; HBE – Hypotension bradycardia episode; HR – Heart rate; ISB – Interscalene block; MBP – Mean blood pressure; PVI – Prophylactic vasopressor infusion; rSO_2 – Regional oxygen saturation of brain; SD – Standard deviation; $SjvO_2$ – Jugular venous oxygen saturation; TIVA – Total intravenous anaesthesia; [a]Liguori *et al*., defined HBE as HR <50 beats/min at anytime or <30 beats in <5 min compared to pre-anaesthetic state with or without hypotension, and/or decrease in SBP >30 mmHg in <5 min compared to pre-anaesthetic values, or any SBP decrease <90 mmHg; necessarily treated by ephedrine, epinephrine or atropine. [b,c]data for early, mid and delayed heart rate [d]equivalent doses [e]data not included for total *n* of meta-analysis. [f]GRADE for primary outcomes

study controls[29,30,33-35,37,39-43,48-63] and randomised trials[4,6,12,13,15,16,26-30,33-35,37-39,41,42,44-47,50,55,60,61,64] were analysed separately [Table 2]. Meta-regression was performed since primary outcomes, characterised by significant heterogeneity, yielded statistically significant omnibus *P* values for statistical models considering different maintenance agents and opioids.

With regard to EHR,[6,15,16,29,33-35,37-40,42-47,49,51,52,54-58,65] MHR[16,29,33-36,38,41,43,46,48-51,53-64,66] and DHR[6,16,29,30,38,43,46,47,49,51,55,56,60,65] responses, meta-analysis showed a statistically significant fall in HR in subjects with GA (GA or GA + RA, $P < 0.0001$). Sensitivity analysis and meta-regressions confirmed that fentanyl significantly influenced the HR drop over time (meta-regression, estimates, 14.8, 9.8 and 16.9; standard error (SE) 5.3, 4.3 and 2.8; $P = 0.007$, 0.024 and <0.001; for early, mid and delayed periods, respectively) in GA subjects (Omnibus $P < 0.001$. Also, refer 'publication bias', Supplementary Digital Content File 5).

Secondary outcomes

BP responses

BP responses were analysed from 67 SGs.[4,6,12,13,15,16,28-38,40,41,44-46,49-56,60,61,64,66] Seven subjects were excluded from the primary study[16,46,58,66] even before surgery due to severe hypotension after BCP. For treatment of hypotension, ephedrine,[4,6,12,13,16,28,32,35,36,44,45,49,52,60] phenylephrine[53,56,60,62,66] or combination of both[29,39-42,46,48,54,59,61,63,65] were used. Less frequently used were cafedrine/theodrenaline,[30,37] epinephrine,[26,31,43] norepinephrine[64] and metaraminol.[15,50] Number of subjects showing drop in BP was a better predictor for hypotension than absolute values. Supplementary Digital Content File 6 describes the details of hypotension with respect to type of anaesthesia or maintainance agent used at BCP.

CDEs

CDEs were evaluated in 33SGs.[15,16,33-35,39,45,46,48,53,58-61,64,65] Meta-analysis of pooled estimates showed statistically significant fall in absolute values of rSO_2 with both TIVA-propofol[33,35,52,59,61] and inhalational[15,16,35,39,45,46,48,53,58,60,64,65] maintenance anaesthetics ($P < 0.00001$). There were no differences between sub-groups with respect to the type of maintenance agent used ($P = 0.05$). Lowest recorded values of CDEs[33-35,39,45-47,53,59,60,65] and data on number of subjects who experienced CDEs[6,33,34,39,43,46,59-61,64,65] are detailed in Supplementary Digital Content File 7.

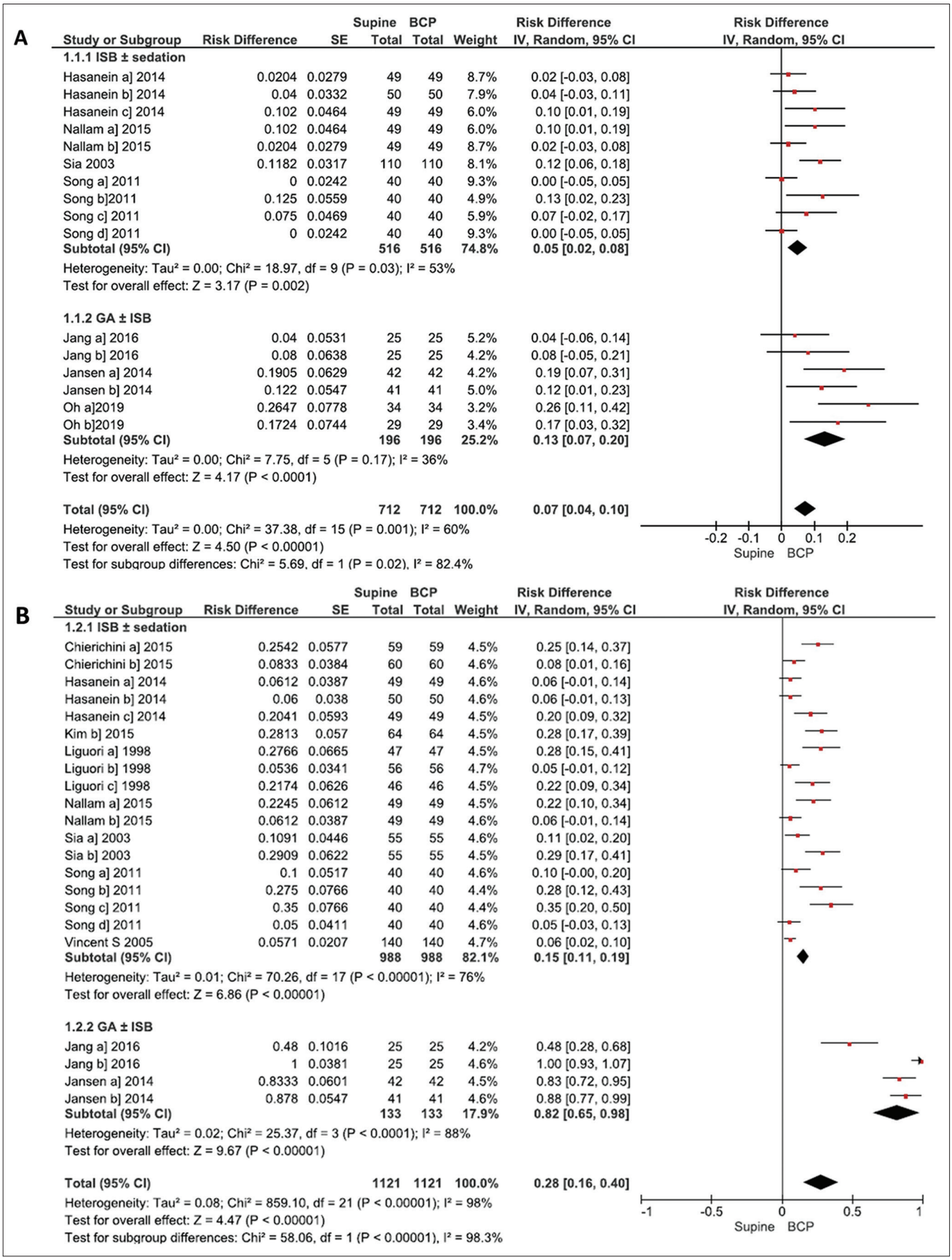


Figure 1: Bradycardia (A) and HBE (B) meta-analysis forest plots. All hypotension incidences were included. BCP – Beach chair position; CI-Confidence interval; GA – General anaesthesia; HBE - Hypotension-bradycardia episode; ISB – Interscalene block; IV- Inverse variance; SE -Standard error

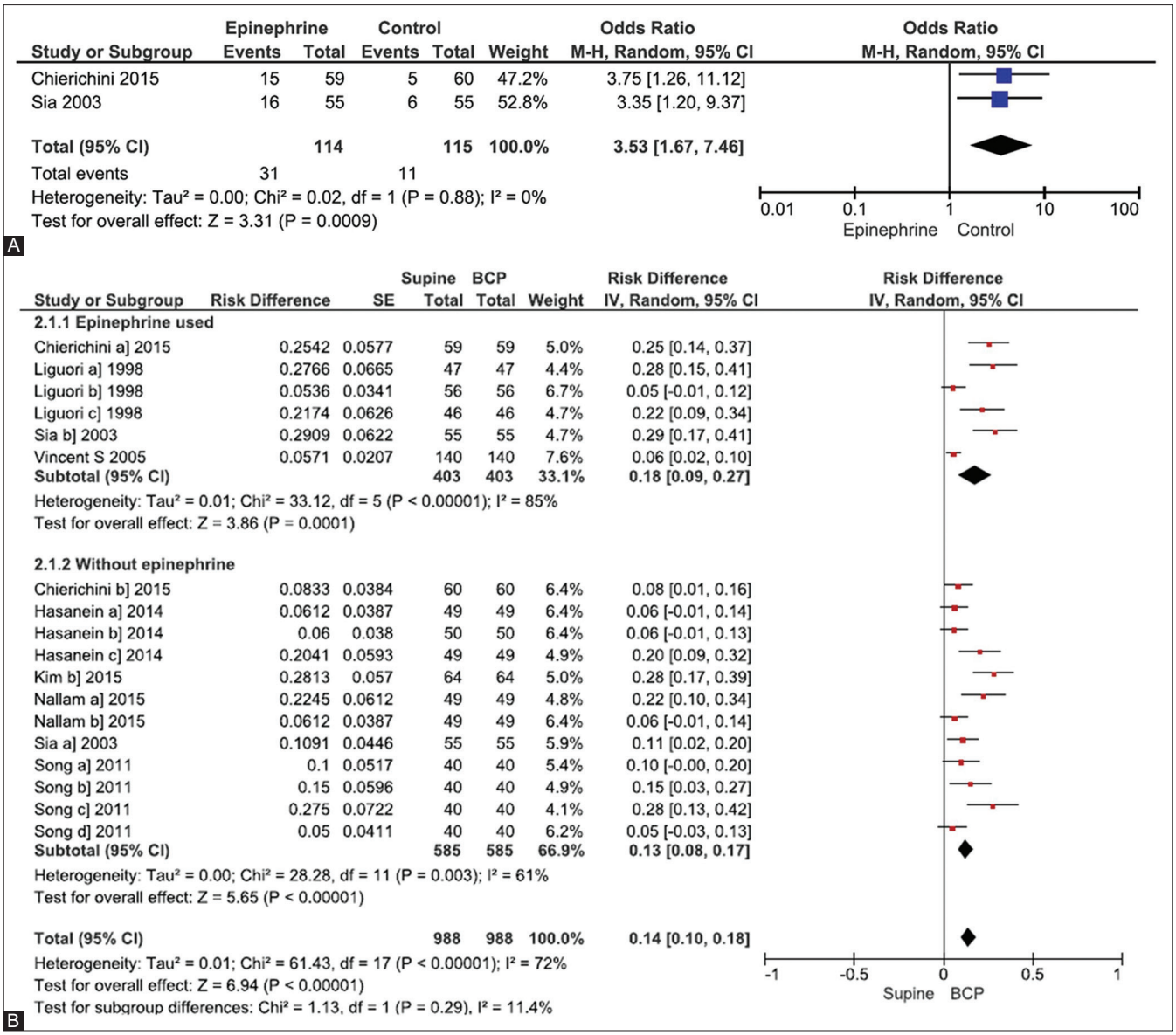


Figure 2: Effect of β-agonists (epinephrine) on bradycardia/HBEs. A. Forest plot for the use of epinephrine. B. Subgroup analysis forest plots for sub-groups using epinephrine and for those without. GA subjects are not included in this analysis. BCP - Beach chair position; CI - Confidence interval; GA – General anaesthesia; HBE - Hypotension-bradycardia episode; IV - Inverse variance. M-H - Mantel-Haenszel

Relationship between rSO_2, $SjvO_2$ and HR

Seventeen SGs[33-35,46,56,60,65] evaluated the HR and rSO_2 at specific intervals over the entire BCP period. Data were recorded as statistical averages for absolute values of consecutive timings. Meta-correlation-analysis showed correlation between the HR and rSO_2 values ($r = 0.608$, 95%CI, 0.439 to 0.735, $P < 0.001$). Correlation was attempted between HR and $SjvO_2$ absolute values from 12SGs.[16,33-35] Meta-correlation analysis revealed statistically significant but weak parallel correlation ($r = 0.397$, 95%CI, 0.151 to 0.597, $P < 0.001$) indicating an association between HR and $SjvO_2$ values [Figure 5].

Use of PVIs and effect on HR, rSO_2 and HR-rSO_2 relationships,[15,33-35] details of physiological controls,[31,53,59,62] vaso-active drugs consumption[16,33,35,40,44,48,54,56,60,62] are detailed elsewhere (Footnote of Supplementary Digital Content File 3).

DISCUSSION

In our meta-analysis, we attempted to find the incidence and associations of adverse HR-responses during shoulder surgeries done in BCP. We observed the incidence of isolated bradycardia and HBE to be 9.1% and 14.9%, respectively. Current literature

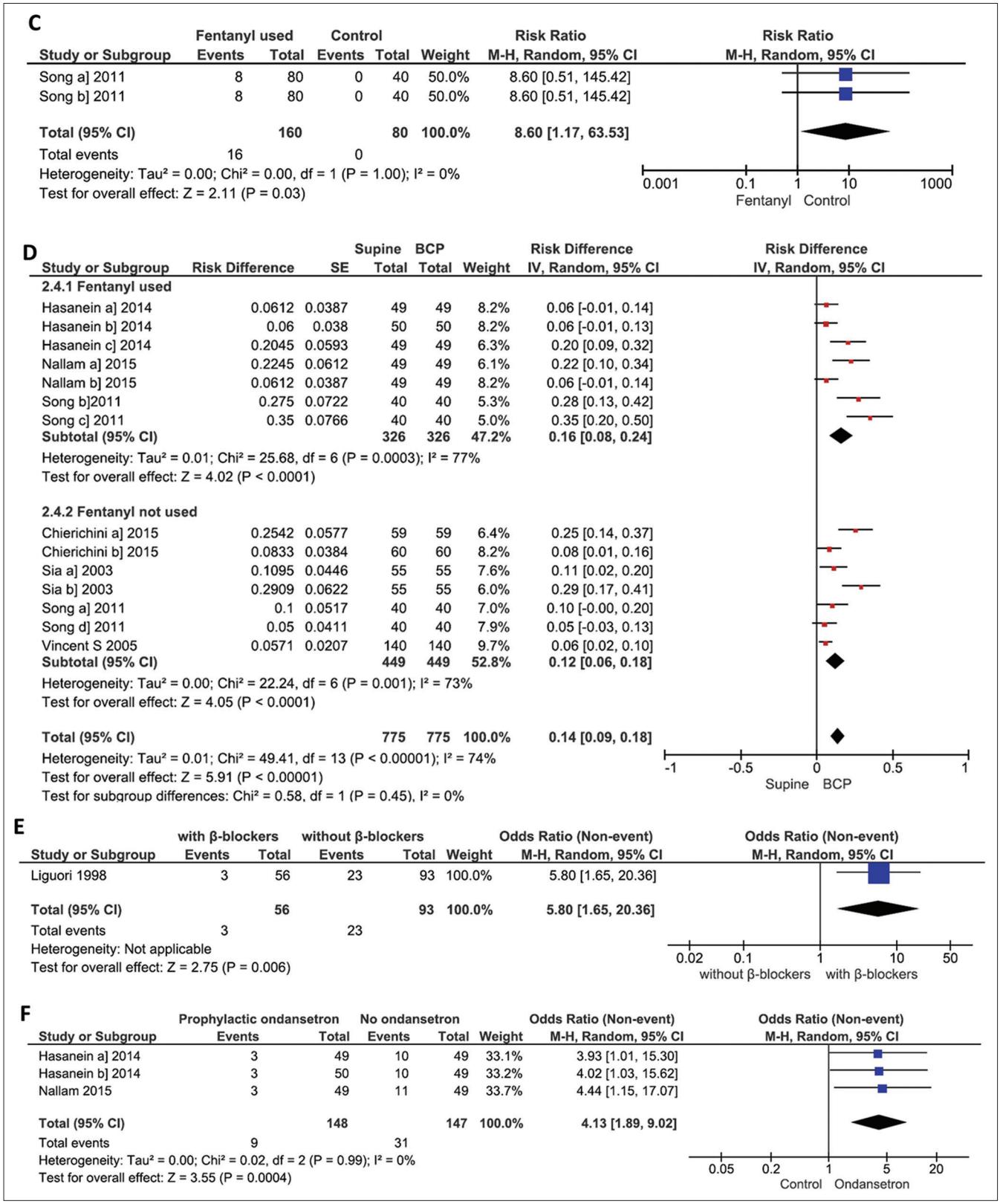


Figure 3: Effect of drugs that can modify incidence of bradycardia/HBEs. Forest plots for fentanyl (C, D), ß-blockers (E) and ondansetron (F) on bradycardia/HBEs. GA subjects are not included in this analysis. BCP - Beach chair position; CI - Confidence interval; GA – General anaesthesia; IV - Inverse variance. M-H - Mantel-Haenszel

provides no concrete evidence linking different anaesthetic techniques, β-agonists or fentanyl with adverse HR-responses. Trials confirming the protective effects of ondansetron and β-blockers against HBEs

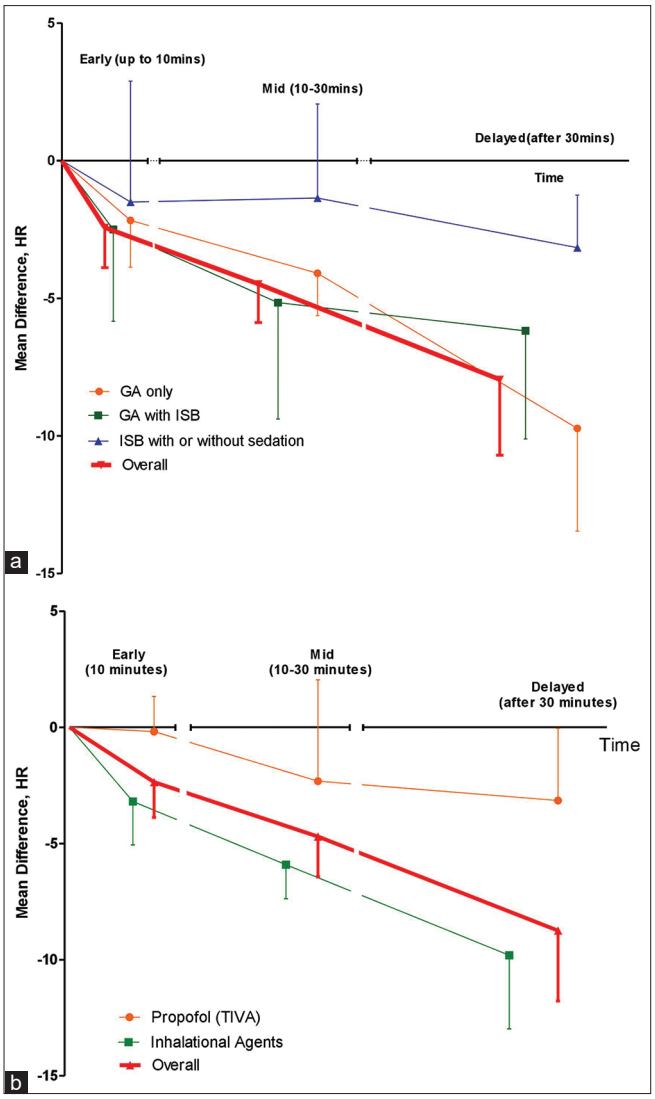


Figure 4: Fall of HR over time, for pooled serial measurements under anaesthesia. The mean differences (MDs) are studied for the first 10 minutes, 11-30 minutes and after 30 minutes of beach-chair position from pre-BCP levels. For different types of anaesthesia (a) and maintenance agents (b), the trends are shown. GA - General anaesthesia; ISB - Interscalene block; TIVA - Total intravenous anaesthesia

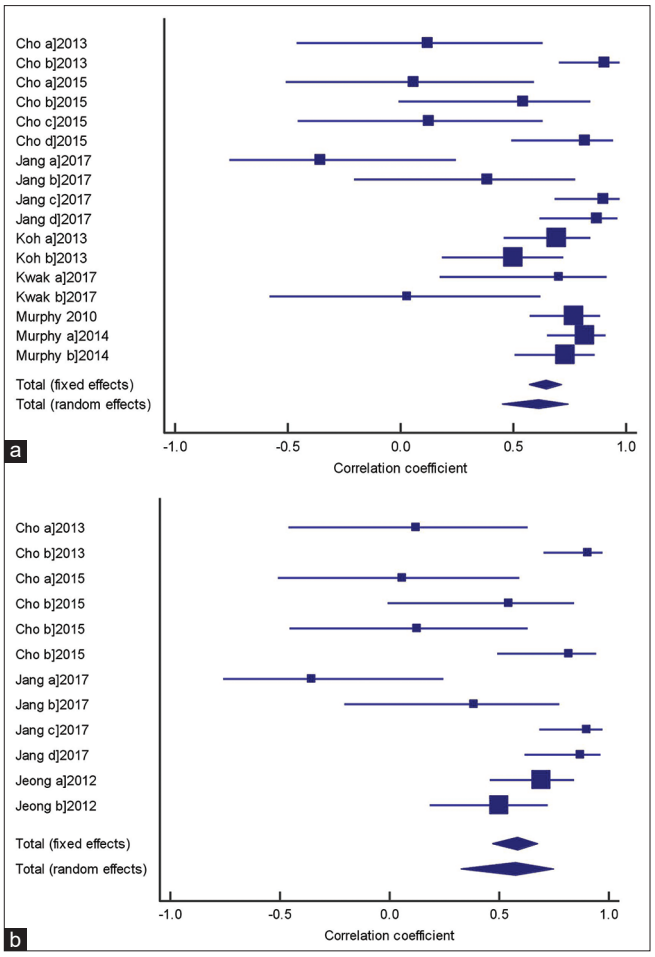


Figure 5: Meta-correlation-analysis depicting the relationship between rSO_2 (a), $SjvO_2$ (b) and HR. 95% confidence intervals are shown. HR - Heart rate; rSO_2- Regional cerebral oxygen saturation; $SjvO_2$ - Jugular venous oxygen saturation

are few in number. Our meta-analysis unequivocally confirms the influence of fentanyl on HR-drop over time in BCP-GA subjects. Furthermore, HR-rSO_2/$SjvO_2$ relationships in GA subjects are clearly elucidated.

The interpretations of adverse HR events may differ between GA and ISB subjects. The seemingly excessive risk of adverse events for GA over ISB subjects could be fallacious for several reasons. Anaesthetic or sedation related events, differences in incidence reporting among the included studies significantly influenced the data. Several authors have followed the definition of Liguori and colleagues,[26] where hypotension in isolation is considered an 'adverse event'. Sub-group meta-analysis has excluded ones that may have reported hypotension but not as a 'true' event of adverse HR-response. To avoid overlapping terms of these cardiovascular events, we analysed them separately. Any conclusion as to whether the hypotension/HBE event was directly linked to BCP or anaesthetic/non-anaesthetic agents remained elusive after this analysis, since every individual received a pharmacological agent in one form or the other. Inclusion of ISB subjects alone to account for adverse HR-responses was likely to reflect the true incidences. Presuming that every event was not the 'true' bradycardia/HBE among all, the actual incidence of bradycardia/HBE therefore, could be less than estimated.

The adverse HR-events were observed approximately between 10 to 50 minutes. Mechanisms related to peak plasma levels of local anaesthetics after ISB or blockade

Table 2: Sensitivity analysis

Factor/Covariate	Time	Number of subjects	Mean difference, HR (95% confidence interval)	I^2	*P** for χ^2 heterogeneity	*P*, overall effect	Number of study groups
Use of PVIs	Early	107	3.67 (-2.4, 9.7)	83%	***<0.00001***	0.23	7
	Mid	58	-0.81 (-4.39, 2.78)	0%	0.94	0.66	3
Inducing agent, Propofol	Early	1333	2.72 (1.21, 4.23)	79%	***<0.00001***	***0.0005***	46
Inducing agent, Thiopentone	Early	120	2.18 (-0.95, 5.3)	0%	0.98	0.17	5
Remifentanil	Early	811	2.16 (0.35, 3.96)	79%	***<0.00001***	***0.02***	27
	Mid	444	5.62 (1.99, 9.25)	83%	***<0.00001***	***0.002***	18
	Delayed	229	8.8 (5.41, 12.18)	50%	0.05	***<0.00001***	8
Fentanyl	Early	111	6.02 (2.28,9.76)	78%	***<0.00001***	***0.002***	11
	Mid	296	6.98 (4.95,9.01)	0%	0.74	***<0.00001***	11
	Delayed	110	16.61 (13.01,20.21)	61%	***0.03***	***<0.00001***	5
Alfentanil	Early	80	4.59 (-1.03,10.22)	61%	0.05	0.11	4
	Mid	80	3.13 (-0.45,6.70)	0%	0.66	0.09	4
	Delayed	40	2.93 (-1.53,7.39)	0%	0.63	0.2	2
Sufentanil	Early	53	-0.8 (-5.41, 3.81)	NA	NA	0.73	1
	Mid	117	0.63 (-1.96,3.21)	0%	0.61	0.63	4
TIVA, propofol	Early	480	0.59 (-0.93,2.10)	0%	0.88	0.45	13
	Mid	340	2.72 (-1.64,7.07)	85%	***<0.00001***	0.22	15
	Delayed	100	3.55 (0.46,6.64)	0%	0.86	***0.02***	3
Sevoflurane	Early	826	3.55 (1.56, 5.53)	84%	***<0.00001***	***0.0005***	33
	Mid	736	5.84 (4.23, 7.45)	39%	***0.02***	***<0.00001***	27
	Delayed	420	9.54 (5.9, 13.2)	83%	***<0.00001***	***<0.00001***	16
Desflurane	Early	87	2.04 (-1.18, 5.25)	0%	0.89	0.21	4
	Mid	106	7.32 (3.64, 10.99)	40%	0.16	***<0.0001***	5
	Delayed	60	13.3 (9.72, 16.88)	0%	0.5	***<0.00001***	3
Randomised trials	Early	1072	2.41 (0.69, 4.14)	80%	***<0.00001***	***0.006***	41
	Mid	649	4.33 (2.81, 5.84)	27%	0.08	***<0.00001***	32
	Delayed	530	9.35 (6.09, 12.61)	82%	***<0.00001***	***<0.00001***	20
Study Controls	Early	709	1.73 (0.03, 3.43)	32%	0.07	0.05	23
	Mid	776	6.09 (3.54, 8.65)	75%	***<0.00001***	***<0.00001***	26
	Delayed	361	8.84 (5.78, 11.89)	61%	***0.003***	***<0.00001***	12

PVI – Prophylactic vasopressor infusion; TIVA – Total intravenous anaesthesia; HR – Heart rate; χ^2-Chi-square; *critical *P*=0.05; significant *P* are bold and italicised

of cardiac sympathetic nerves via stellate ganglion were described. However, these mechanisms do not explain the adverse HR-responses in GA subjects. The claim in few trials regarding the augmentation of HBE risk by epinephrine has been with very low evidence. Epinephrine was administered either through skin infiltration, saline irrigation, concomitant to local anaesthetic or intra-articular injections. One study compared epinephrine to norepinephrine to study HBEs without a control group.[6] The paucity of data with respect to number of studies or type of drug (local anaesthetics, beta-agonists etc.) poses a limitation to any conclusion regarding risk modifying drugs. The factors like variable plasma levels with different routes of administration, short half-life etc., will not favour the specific timings of adverse events. Furthermore, we could not demonstrate higher incidences of adverse HR-responses for the fentanyl SGs over no-fentanyl in ISB subjects. Earlier studies have reported a dose-dependent increase in bradycardia/HBE incidences with fentanyl in BCP-cohorts.[8,12] The effects of fentanyl on HR were further validated by our second analysis of this study as we observed the highest HR-fall occurring with the use of fentanyl. Fentanyl acts on μ-opioid receptors on cardiac vagal neurons in the nucleus ambiguus and neurons preceding them to reduce GABAergic neurotransmission and induce bradycardia.[12] We believe, therefore, that adverse HR-response could be easily augmented with fentanyl use.

Association between CDEs and HR is as yet unreported. While HR is believed to be influenced by hypoxic events, defining HR-rSO_2 relationship is not easy. Cerebral oxygenation may involve regional differences. The near-infrared reflectance spectroscopy is usually applied to frontal areas for convenience while actual rSO_2 at the medullary vasomotor centre (VMC) is un-monitored. We have demonstrated a HR-rSO_2/$SjvO_2$ association through meta-correlation analysis. There is a

dearth of literature on monitoring rSO_2 during the ISB-BCP surgery with none reporting any adverse HR-responses. CDEs in ISB-BCP patients have been reported as incidences of 10%,[67] 3.3%[56] or lower absolute values of rSO_2.[68] Higher partial pressures of oxygen during controlled ventilation may decrease the CDEs compared to spontaneously breathing (but sedated) ISB subjects. CDEs reported by Yadeau and colleagues[67] in RA patients showed no correlation with all hypotensive events. All ISB studies reporting bradycardia/HBE received intravenous fentanyl and midazolam singly or in combination. Furthermore, propofol infusion (sedation), β-blockers and oxygen (discretional) were randomly used in ISB subjects of this meta-analysis. Adverse HR-responses observed in ISB subjects, therefore, could be secondary to sedation and its CDE effects.[69]

We have limitations for our meta-analysis. From the available studies, we were unable to describe emergent strategy for preventing and managing adverse HR-responses during BCP-surgery, which is needed to inform practice. Non-availability of raw patient data or lowest achieved HR data for many trials precluded conducting individual patient meta-analysis or correlations. Heterogeneity is high in our study but we consider this acceptable since the pre-defined eligibility criteria for the meta-analysis are sound and the data are correct. While included trials might have allocated treatment randomly, their SGs inclusion in this review has not been random. Publication bias was minimal. However, inclusions of studies to this review were not based on Jadad scores.

CONCLUSIONS

Amalgamating the diverse and selective reporting of HR-responses in literature on shoulder surgeries in BCP, we observed lack of enough evidence for definitive associations of adverse HR-responses with different pharmacological agents like β-agonists or opioids. However, fentanyl can significantly influence HR-fall in BCP. Since HR-variations correlate well with monitored brain saturation values, the adverse HR-responses may also be induced by regional oxygenation of VMC in the brain, independent of anaesthetic agents. Close monitoring for CDEs could free the anaesthesiologist from concerns regarding the type of anaesthesia as well as intra-operative maintenance anaesthetic agents and ancillary drugs employed. However, further studies are essential to derive a cause-effect relationship with respect to adverse HR-responses. The key may lie in cerebral oxygenation levels at the VMC, and monitoring this parameter could set the direction for future research in this field.

Acknowledgements

We sincerely acknowledge Dr Rajani Kadri, M.S., Associate Professor, Department of Opthalmology, A J I M S & Research Centre, Mangalore for her excellent support, contribution and cooperation during the preparation of manuscript. We also thank Mr. Naveen Mishra, Pranavi and Poorvi for their kind help during manuscript preperation.

Financial support and sponsorship

Grants, sponsors, and funding sources that provided direct financial support to the research work contained in the manuscript: None declared for all above mentioned authors.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

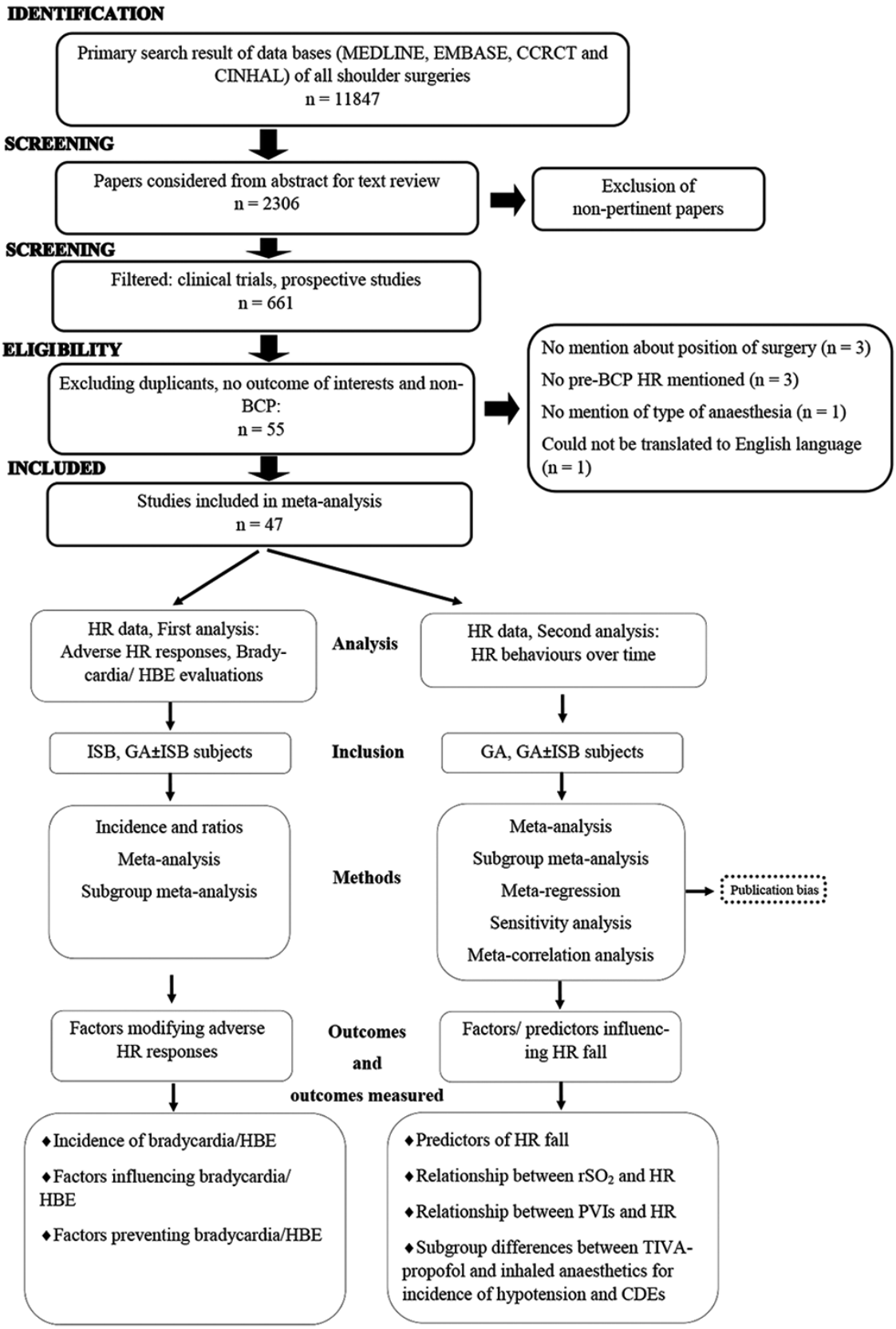
1. So J, Shin WJ, Shim JH. A cardiovascular collapse occurred in the beach chair position for shoulder arthroscopy under general anesthesia -A case report. Korean J Anesthesiol 2013;64:265-7.
2. D'Alessio JG, Weller RS, Rosenblum M. Activation of the Bezold-Jarisch reflex in the sitting position for shoulder arthroscopy using interscalene block. Anesth Analg 1995;80:1158-62.
3. Harper S. A hypotensive/bradycardic episode leading to asystole in a patient undergoing shoulder arthroscopy in the sitting position with interscalene block and intravenous sedation: A case report. AANA J 2016;84:27-33.
4. Sia S, Sarro F, Lepri A, Bartoli M. The effect of exogenous epinephrine on the incidence of hypotensive/bradycardic events during shoulder surgery in the sitting position during interscalene block. Anesth Analg 2003;97:583-8.
5. Song SY, Roh WS. Hypotensive bradycardic events during shoulder arthroscopic surgery under interscalene brachial plexus blocks. Korean J Anesthesiol 2012;62:209-19.
6. Chierichini A, Frassanito L, Vergari A, Santoprete S, Chiarotti F, Saccomanno MF, *et al*. The effect of norepinephrine versus epinephrine in irrigation fluid on the incidence of hypotensive/bradycardic events during arthroscopic rotator cuff repair with interscalene block in the sitting position. Arthroscopy 2015;31:800-6.
7. Lee HW. Hypotensive and bradycardic episodes in the sitting position during shoulder arthroscopy using interscalene block: Can those be alerted? Korean J Anesthesiol 2010;58:1-3.
8. Seo KC, Park JS, Roh WS. Factors contributing to episodes of bradycardia hypotension during shoulder arthroscopic surgery in the sitting position after interscalene block. Korean J Anesthesiol 2010;58:38-44.
9. Liu JE, Hahn RT, Stein KM, Markowitz SM, Okin PM, Devereux RB, *et al*. Left ventricular geometry and function

preceding neurally mediated syncope. Circulation 2000;101:777-83.
10. Novak V, Honos G, Schondorf R. Is the heart 'empty' at syncope? J Auton Nerv Syst 1996;60:83-92.
11. Campagna JA, Carter C. Clinical relevance of the Bezold-Jarisch reflex. Anesthesiology 2003;98:1250-60.
12. Song SY, Son SH, Kim SO, Roh WS. Intravenous fentanyl during shoulder arthroscopic surgery in the sitting position after interscalene block increases the incidence of episodes of bradycardia hypotension. Korean J Anesthesiol 2011;60:344-50.
13. Nallam SR, Dara S. Effect of intravenous ondansetron on reducing the incidence of hypotension and bradycardia events during shoulder arthroscopy in sitting position under interscalene brachial plexus block: A prospective randomized trial. Indian J Anaesth 2015;59:353-8.
14. Lee JH, Min KT, Chun YM, Kim EJ, Choi SH. Effects of beach-chair position and induced hypotension on cerebral oxygen saturation in patients undergoing arthroscopic shoulder surgery. Arthroscopy 2011;27:889-94.
15. Soeding PF, Hoy S, Hoy G, Evans M, Royse CF. Effect of phenylephrine on the haemodynamic state and cerebral oxygen saturation during anaesthesia in the upright position. Br J Anaesth 2013;111:229-34.
16. Jeong H, Jeong S, Lim HJ, Lee J, Yoo KY. Cerebral oxygen saturation measured by near-infrared spectroscopy and jugular venous bulb oxygen saturation during arthroscopic shoulder surgery in beach chair position under sevoflurane-nitrous oxide or propofol-remifentanil anesthesia. Anesthesiology 2012;116:1047-56.
17. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, *et al*. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. PLoS Med 2009;6:e1000100.
18. Higgins-Julian PT, Altman DG, Gøtzsche-Peter C, Peter J, David M, Andrew OD, *et al*. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343:d5928.
19. Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. The Cochrane Collaboration, 2011. Available from: www.handbook.cochrane.org. [Last updated on 2011 Mar].
20. Sedgwick P. Intention to treat analysis versus per protocol analysis of trial data. BMJ. 2015;350:h681.
21. Saravanan S, Kocarev M, Wilson RC, Watkins E, Columb MO, Lyons G. Equivalent dose of ephedrine and phenylephrine in the prevention of post-spinal hypotension in caesarean section. Br J Anaesth 2006;96:95–9.
22. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002;21:1539-58.
23. Thompson SG, Higgins JP. How should meta-regression analyses be undertaken and interpreted? Stat Med 2002;21:1559-73.
24. Higgins JP, White IR, Anzures-Cabrera J. Meta-analysis of skewed data: Combining results reported on log-transformed or raw scales. Stat Med 2008;27:6072-92.
25. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629-34.
26. Liguori GA, Kahn RL, Gordon J, Gordon MA, Urban MK. The use of metoprolol and glycopyrrolate to prevent hypotensive/bradycardic events during shoulder arthroscopy in the sitting position under interscalene block. Anesth Analg 1998;87:1320-5.
27. Oh CS, Sa M, Park HJ, Piao L, Oh KS, Kim SH. Effects of remote ischemic preconditioning on regional cerebral oxygen saturation in patients in the beach chair position during shoulder surgery: A double-blind randomized controlled trial. J Clin Anesth 2020;61:109661.
28. Hasanein R, El-Syed W. The effect of ondansetron in preventing the hypotensive bradycardic events during shoulder arthroscopy done under interscalene block in the sitting position. Egypt J Anaesth 2014;30:305-10.
29. Jang J, Hwang S, Hwang J, Kim Y, Sohn J, Lee J. The effect of dexmedetomidine on S-100 β in beach chair position for arthroscopic shoulder surgery. A randomized controlled trial. Int J Clin Exp Med 2016;9:18772-9.
30. Janssen H, Stosch Rv, Pöschl R, Büttner B, Bauer M, Hinz JM, *et al*. Blood pressure response to combined general anaesthesia/interscalene brachial plexus block for outpatient shoulder arthroscopy. BMC Anesthesiol 2014;14:50-8.
31. Kim JH, Song SY, Ryu T, Choi CH, Sung SY, Roh WS. Changes in heart rate variability after sitting following interscalene block. Clin Auton Res 2015;25:327-33.
32. Vincent S, Laurent D, Francis B. Sedation with target-controlled propofol infusion during shoulder surgery under interscalene brachial plexus block in the sitting position: Report of a series of 140 patients. Eur J Anaesthesiol 2005;22:853-7.
33. Cho SY, Kim SJ, Jeong CW, Jeong CY, Chung SS, Lee J, *et al*. Under general anesthesia arginine vasopressin prevents hypotension but impairs cerebral oxygenation during arthroscopic shoulder surgery in the beach chair position. Anesth Analg 2013;117:1436-43.
34. Cho SY, Kim J, Park SH, Jeong S, Chung SS, Yoo KY. Vasopressin ameliorates hypotension induced by beach chair positioning in a dose-dependent manner in patients undergoing arthroscopic shoulder surgery under general anesthesia. Korean J Anesthesiol 2015;68:232-40.
35. Jang EA, Song JA, Shin JY, Yoon JJ, Yoo KY, Jeong S. Background anaesthetic agents do not influence the impact of arginine vasopressin on haemodynamic states and cerebral oxygenation during shoulder surgery in the beach chair position: A prospective, single-blind study. BMC Anesthesiol 2017;17:73-84.
36. Larsen SL, Lyngeraa TS, Maschmann CP, Van Lieshout JJ, Pott FC. Cardiovascular consequence of reclining vs. sitting beach-chair body position for induction of anesthesia. Front Physiol 2014;5:187-92.
37. Schotola H, Kirsch KC, Höcker J, Egan M, Büttner B, Wiese C, *et al*. Ketamine in outpatient arthroscopic shoulder surgery: Effects on postoperative pain, hemodynamic stability and process times. Open Med (Wars) 2015;10:297-305.
38. Bengisun ZK, Ekmekçi P, Akan B, Köroğlu A, Tüzüner F. The effect of adding dexmedetomidine to levobupivacaine for interscalene block for postoperative pain management after arthroscopic shoulder surgery. Clin J Pain 2014;30:1057-61.
39. Cox RM, Jamgochian GC, Nicholson K, Wong JC, Namdari S, Abboud JA. The effectiveness of cerebral oxygenation monitoring during arthroscopic shoulder surgery in the beach chair position: A randomized blinded study. J Shoulder Elbow Surg 2018;27:692-700.
40. Jo YY, Jung WS, Kim HS, Chang YJ, Kwak HJ. Prediction of hypotension in the beach chair position during shoulder arthroscopy using pre-operative hemodynamic variables. J Clin Monit Comput 2014;28:173-8.
41. Jung W, Kim H, Kim J, Park YS, Kwak HJ. Cardiopulmonary effect of the beach-chair position in shoulder surgery: A comparison between sevoflurane and propofol. Korean J Anesthesiol 2007;52:23-8.
42. Kim JY, Lee JS, Lee KC, Kim HS, Park CH, Kwak HJ. The effect of sequential compression device on hypotension in the sitting position during shoulder arthroscopy; A comparison with elastic stocking. Korean J Anesthesiol 2009;57:417-21.
43. Kocaoglu B, Ozgen SU, Toraman F, Karahan M, Guven O. Foreseeing the danger in the beach chair position: Are standard measurement methods reliable? Knee Surg Sports Traumatol Arthrosc 2015;23:2639-44.
44. Kwak HJ, Lee JS, Lee DC, Kim HS, Kim JY. The effect of a sequential compression device on hemodynamics in

arthroscopic shoulder surgery using beach-chair position. Arthroscopy 2010;26:729-33.
45. Kwak HJ, Lee D, Lee YW, Yu GY, Shinn HK, Kim JY. The intermittent sequential compression device on the lower extremities attenuates the decrease in regional cerebral oxygen saturation during sitting position under sevoflurane anesthesia. J Neurosurg Anesthesiol 2011;23:1-5.
46. Kwak HJ, Lee JY, Wha LJ, Kim HS, Hur HJ, Kim JY. Effect of mild hypercapnia on lung oxygenation in sitting position during shoulder arthroscopy under general anesthesia. Med Sci Monit 2017;23:843-9.
47. Maghawry KM, El-Agamy AE, Tahir WI, Zein AF. Cerebral oxygen saturation monitoring during hypotensive anesthesia in shoulder arthroscopy: A comparative study between dexmedetomidine and esmolol. Egypt J Anaesth 2015;31:43-52.
48. Mori Y, Yamada M, Akahori T, Hatakeyama N, Yamazaki M, Fujiwara Y, *et al*. Cerebral oxygenation in the beach chair position before and during general anesthesia in patients with and without cardiovascular risk factors. J Clin Anesth 2015;27:457-62.
49. Ozturk L, Kesimci E, Albayrak T, Kanbak O. Bispectral index-guided general anaesthesia in combination with interscalene block reduces desflurane consumption in arthroscopic shoulder surgery: A clinical comparison of bupivacaine versus levobupivacaine. BMC Anesthesiol 2015;15:104-11.
50. Soeding PF, Wang J, Hoy G, Jarman P, Phillips H, Marks P, *et al*. The effect of the sitting upright or 'beachchair' position on cerebral blood flow during anaesthesia for shoulder surgery. Anaesth Intensive Care 2011;39:440-8.
51. Basaran B, Yilbas AA, Gultekin Z. Effect of interscalene block on intraocular pressure and ocular perfusion pressure. BMC Anesthesiol 2017;17:144-50.
52. Choi JC, Lee JH, Lee YD, Kim SY, Chang SJ. Ankle-brachial blood pressure differences in the beach-chair position of the shoulder surgery. Korean J Anesthesiol 2012;63:515-20.
53. Closhen D, Berres M, Werner C, Engelhard K, Schramm P. Influence of beach chair position on cerebral oxygen saturation: A comparison of INVOS and FORE-SIGHT cerebral oximeter. J Neurosurg Anesthesiol 2013;25:414-9.
54. Hanouz JL, Fiant AL, Gérard JL. Middle cerebral artery blood flow velocity during beach chair position for shoulder surgery under general anesthesia. J Clin Anesth 2016;33:31-6.
55. Jo YY, Kim HS, Chang YJ, Yun SY, Kwak HJ. The effect of warmed inspired gases on body temperature during arthroscopic shoulder surgery under general anesthesia. Korean J Anesthesiol 2013;65:14-8.
56. Koh JL, Levin SD, Chehab EL, Murphy GS. Neer Award 2012: Cerebral oxygenation in the beach chair position: A prospective study on the effect of general anesthesia compared with regional anesthesia and sedation. J Shoulder Elbow Surg 2013;22:1325-31.
57. Lee SW, Choi SE, Han JH, Park SW, Kang WJ, Choi YK. Effect of beach chair position on bispectral index values during arthroscopic shoulder surgery. Korean J Anesthesiol 2014;67:235-9.
58. Lee SH, Chun YM, Oh YJ, Shin S, Park SJ, Kim SY, *et al*. Prediction of fluid responsiveness in the beach chair position using dynamic preload indices. J Clin Monit Comput 2016;30:995-1002.
59. Meex I, Vundelinckx J, Buyse K, Deburggraeve F, De Naeyer S, Desloovere V, *et al*. Cerebral tissue oxygen saturation values in volunteers and patients in the lateral decubitus and beach chair positions: A prospective observational study. Can J Anaesth 2016;63:537-43.
60. Murphy GS, Szokol JW, Avram MJ, Greenberg SB, Shear TD, Vender JS, *et al*. Effect of ventilation on cerebral oxygenation in patients undergoing surgery in the beach chair position: A randomized controlled trial. Br J Anaesth 2014;113:618-27.
61. Picton P, Dering A, Alexander A, Neff M, Miller BS, Shanks A, *et al*. Influence of ventilation strategies and anesthetic techniques on regional cerebral oximetry in the beach chair position: A prospective interventional study with a randomized comparison of two anesthetics. Anesthesiology 2015;123:765-74.
62. Tange K, Kinoshita H, Minonishi T, Hatakeyama N, Matsuda N, Yamazaki M, *et al*. Cerebral oxygenation in the beach chair position before and during general anesthesia. Minerva Anestesiol 2010;76:485-90.
63. Zhu R, Atteya G, Shelley KH, Silverman DG, Alian AA. Analysis of plethysmographic waveform changes induced by beach chair positioning under general anesthesia. J Clin Monit Comput 2014;28:591-6.
64. Frey K, Rehm M, Chappell D, Eisenlohr J, Crispin A, Saller T, *et al*. Preemptive volume therapy to prevent hemodynamic changes caused by the beach chair position: Hydroxyethyl starch 130/0.4 versus Ringer's acetate-a controlled randomized trial. J Shoulder Elbow Surg 2018;27:2129-38.
65. Murphy GS, Szokol JW, Marymont JH, Greenberg SB, Avram MJ, Vender JS, *et al*. Cerebral oxygen desaturation events assessed by near-infrared spectroscopy during shoulder arthroscopy in the beach chair and lateral decubitus positions. Anesth Analg 2010;111:496-505.
66. McCulloch TJ, Liyanagama K, Petchell J. Relative hypotension in the beach-chair position: Effects on middle cerebral artery blood velocity. Anaesth Intensive Care 2010;38:486-91.
67. Yadeau JT, Liu SS, Bang H, Shaw PM, Wilfred SE, Shetty T, *et al*. Cerebral oximetry desaturation during shoulder surgery performed in a sitting position under regional anesthesia. Can J Anaesth 2011;58:986-92.
68. Drenjančević HI, Drenjančević D, Davidović-Cvetko E, Drenjančević I, Gulam D, Kvolik S. Does the anesthesia technique affect arterial pressure and regional cerebral oxygen saturation during shoulder arthroscopy in the beach chair position? Acta Clin Croat 2018;57:473-9.
69. Kinsella SM, Tuckey JP. Perioperative bradycardia and asystole: Relationship to vasovagal syncope and the Bezold-Jarisch reflex. Br J Anaesth 2001;86:859-68.

1. Beach chair position
2. Beach-chair position
3. BCP
4. BCP complication
5. BCP complications
6. BCP anaesthesia
7. BCP anesthesia
8. Beach chair seated positioning
9. Beach chair seated anaesthesia
10. Beach chair seated surgery
11. OR/1 to 10 (3235)
12. Shoulder arthroscopy
13. Shoulder arthroplasty
14. Shoulder arthroscopic surgery
15. Shoulder surgery
16. Shoulder scopy
17. OR/12 to 16 (37477)
18. Hemodynamic
19. Hemodynamic monitoring
20. Hemodynamic/clinical
21. Hemodynamic/anaesthetic
22. Hemodynamic
23. Haemodynamic monitoring
24. OR/18 to 23 (724087)
25. Heart rate
26. Heart rate response
27. Heart rate responses
28. Adverse hemodynamic events
29. Adverse heart rate response
30. OR/25 to 29 (338011)
31. Hypotensive bradycardic episode
32. Hypotensive bradycardic
33. Hypotensive bradycardic episode
34. Hypotensive bradycardic episodes
35. Hypotensive bradycardic events
36. Bradycardic episode
37. OR/31 to 36 (37)
38. Bezold jarish reflex
39. Bezold jarish reflex activation
40. Bezold jarisch like bradycardia reflex
41. Bezold jarish
42. Bezold jarisch like bradycardia reflex
43. Bezold jarisch reflex like reaction
44. Bezold jarisch effects
45. Bezold jarisch like
46. Bezold jarisch like bradycardia reflex
47. Bezold jarisch like effect
48. Bezold jarisch like phenomenon
49. Bezold jarisch like reflex
50. Bezold jarisch model
51. Bezold jarisch reflex
52. Bezold jarisch reflex activation
53. Bezold jarisch reflex assay
54. Bezold jarisch reflex function
55. Bezold jarisch reflex induced decrease
56. Bezold jarisch reflex responses
57. Bezold jarisch reflex test
58. Bezold jarisch reflexes
59. Bezold jarisch response
60. Bezold jarisch s
61. OR/38 to 53 (377)
62. Bradycardia
63. Bradycardia/arrest
64. Bradycardia/asystole
65. Bradycardia/asystolia
66. Bradycardia/asystolic
67. Bradycardia/atrioventricular
68. Bradycardia/bradyarrhythmia
69. Bradycardia/cardiac
70. Bradycardia/case
71. Bradycardia/complications
72. Bradycardia/collapse
73. Bradycardia/desaturation
74. Bradycardia/hypotension
75. Bradycardia/sinus
76. Bradycardia/sinus arrest
77. Bradycardia/slow
78. Bradycardia/surgery
79. Bradycardia event
80. Bradycardia events
81. OR/62 to 80 (25618)
82. Epinephrine
83. Adrenaline
84. Beta blocker
85. Ondansetron
86. 11 OR 17 OR 24 OR 30 OR 37 OR 61 OR 81 (909292)
87. 17 AND 37 AND 61 (2289)
88. 11 AND 17 (214)
89. 17 AND 81 (45)
90. 17 AND 30 (181)
91. 11 AND 24 (41)
92. 61 AND 81 (118)

Supplementary Digital Content File 1: The Search Strategy. The search terms were used to search databases of MEDLINE, EMBASE, CCRCT and, CINHAL (modified to suit each specific database with abstract, keywords and text with the removal of duplicates)



Supplementary Digital Content File 2: Flow Chart for literature Identification and Study Selection. Details of analysis and outcomes are shown. BCP - Beach chair position; CDE - Cerebral desaturation event; GA - General anaesthesia; HR - Heart rate; HBE - Hypotension-bradycardia episode; ISB - Interscalene block; PVIs - Prophylactic vasopressor infusions; rSO_2 - Regional cerebral oxygen saturation; TIVA - Total intravenous anaesthesia

Sl. No.	Trial no.	Author, year	n	Name of SG	Primary outcome	Age (years)	Duration of anaesthesia/ surgery (minutes)	BCP°	Surgery	HTN/DM/Other (n)	Type of anaesthesia	ASA PS	Induction agent	Maintanance agent	Bolck Localisation	Local anaesthetic drug of ISB	Hypotension preventive measure	Incidence of HBE, n(%)	Incidence of bradycardia, n(%)	Use of anticholinergics	Incidence of hypotension, n(%)	Vaso-active agent	Vasoactive agent, bolus vs infusion	Vasoactive agent usage details	Definition of HBE/ bradycardia (HR, beats/min) or hypotension (mm Hg).	Jadad score
1	1	Basaran et al., 2017[51]	30	Control	ISB effects on IOP	52.6 ± 10.6	NP	NP	Shoulder surgery	0/NP/NP	ISB ± sedation	I-II	Nil	Nil	USG + PNS	15ml 0.5% bupivacaine, 15ml 2% lignocaine	Nil	Nil	Nil	Nil	Nil	NIL	Nil	Nil	NP	-1
2	2	Bengisun et al., a) 2014[38]	25	Control (L)	Effect of dexmedetomidine to LA for ISB for post-operative pain	50.4±12.9	85.9 ± 27	Nil	shoulder arthroscopy	NP	GA + ISB	I-II	Propofol	Sevoflurane	PNS	0.5% levobupivacaine, 100mg, 20 ml + E, 50μg	Nil	Nil	Nil	Nil	Nil	NIL	NP	Nil	MAP >20% decrease from BL	5
3	2	Bengisun et al., b) 2014[38]	23	Study (LD)		55.9 ± 8.5	84.1 ± 33.1	Nil	Shoulder arthroscopy	NP	GA + ISB	I-II	Propofol	Sevoflurane	PNS	0.5% levobupivacaine, 100mg, 20 ml + E, 50μg + Dexmedetomidine, 10μg	Nil	Nil	Nil	Nil	Nil	NIL	NP	Nil	MAP >20% decrease from BL	5
4	3	Cherichini et al., a) 2015[6]	59	NE	Effects on HBE by NE, E of irrigation fluid	57 (44-64)	59.5 ± 17.3	NP	Shoulder arthroscopy	26/6/NP	ISB ± sedation	I-II	Nil	Nil	USG + PNS	13-18ml of ropivacaine, 0.75%	NP	15 (25.4%)	NP	Atropine, 0.5mg	NP	Eph	Bolus	NP	NP	5
5	3	Cherichini et al., b) 2015[6]	60	E		59 (45-66)	57.3 ± 18.7	NP	Shoulder arthroscopy	25/10/NP	ISB ± sedation	I-II	Nil	Nil	USG + PNS	13-18ml of ropivacaine, 0.75%	NP	5 (8.3%)	NP	Atropine, 0.5mg	NP	Eph	Bolus	NP	NP	5
6	4	Cho et al., a) 2013[33]	15	Saline	Vasopressin prophylaxis for BCP induced hypotension	62 (39-73)	199 ± 59	65-75°	Shoulder arthroscopy	5/3/NP	GA, TIVA Propofol	I-III	Propofol	Air, Propofol, Remifentanil	Nil	Nil	Supportive stockings	Nil	Nil	Nil	10 (66%)	Eph	Bolus	16 ± 7 mg[a]	MAP <50	4
7	4	Cho et al., b) 2013[33]	15	AVP		61 (48-70)	221 ± 52	65-75°	Shoulder arthroscopy	5/3/NP	GA, TIVA Propofol	I-III	Propofol	Air, Propofol, Remifentanil	Nil	Nil	Supportive stockings, AVP	Nil	Nil	Nil	2 (13.3%)	Eph	Eph bolus and AVP infusion	8 ± 0 mg[a]	MAP <50	4
8	5	Choi et al., 2012[33]	30	Study	Ankle brachial BP differences	56.8 ± 9.58	NP	>45°	Shoulder surgery	NP	GA	I-II	Thiopentone	Sevoflurane, Remifentanil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	NP	NP	NP	NP	-1
9	6	Cho et al., a) 2015[34]	15	Control, saline	Vasopressin effect on BP	58 ± 10	168 ± 53	65-75°	shoulder arthroscopy	4/5/NP	GA, TIVA Propofol	I-III	Propofol	Propofol, Remifentanil	Nil	Nil	Supportive stockings, ringers solution	Nil	Nil	Nil	11 (73.3%)	Eph, Phe	Bolus	Eph, n = 6; phe, n = 5	MAP <50	2
10	6	Cho et al., b) 2015[34]	15	AVP = 0.025 U/kg		62 ± 7	147 ± 66	65-75°	Shoulder arthroscopy	5/2/unclear	GA, TIVA Propofol	I-III	Propofol	Propofol, Remifentanil	Nil	Nil	Supportive stockings, ringers solution, AVP	Nil	Nil	Nil	6 (40%)	Eph, Phe	Bolus and AVP infusion	Eph, n = 1; phe, n = 3	MAP <50	2
11	6	Cho et al., c) 2015[34]	15	AVP = 0.05 U/kg		65 ± 8	186 ± 59	65-75°	Shoulder arthroscopy	7/1/unclear	GA, TIVA Propofol	I-III	Propofol	Propofol, Remifentanil	Nil	Nil	Supportive stockings, ringers solution, AVP	Nil	Nil	Nil	4 (26.7%)	Eph, Phe	Bolus and AVP infusion	Eph, n = 1; phe, n = 1	MAP <50	2
12	6	Cho et al., d) 2015[34]	15	AVP = 0.075 U/kg		60 ± 8	187 ± 51	65-75°	shoulder arthroscopy	5/3/unclear	GA, TIVA Propofol	I-III	Propofol	Propofol, Remifentanil	Nil	Nil	Supportive stockings, ringers solution, AVP	Nil	Nil	Nil	2 (13.3%)	Eph, Phe	Bolus and AVP infusion	Eph, n = 3; phe, n = 5	MAP <50	2
13	7	Closhen et al., 2013[53]	35	Study	BCP effects on cerebral O_2 saturation	53 ± 15	NP	45-60°	Shoulder surgery	14/3/3	GA	I-III	Propofol	Sufentanil, air, sevoflurane	Nil	Nil	Nil	Nil	Nil	Nil	>22 (>63%)	Phe	Bolus	n = 63%	MAP <70	-1
14	8	Cox et al., a) 2018[39]	20	NIRS aware	Effectiveness of cerebral oxygenation monitoring	55 ± 11	129.8 ± 31.2	NP	Shoulder arthroscopy	NP	GA + ISB	I-III	Propofol	Sevoflurane	USG	0.5% ropivacaine, 2mg dexmeditomidine	Nil	Nil	Nil	Nil	2.9 ± 3.4[b]	Eph, Phe	Bolus	NP	SBP <90	2
15	8	Cox et al.,b) 2018[39]	20	NIRS blind		55 ± 12	128 ± 32.3	NP	Shoulder arthroscopy	NP	GA + ISB	I-III	Propofol	Sevoflurane	USG	0.5% ropivacaine, 2mg dexmeditomidine	Nil	Nil	Nil	Nil	2.3 ± 2.1[b]	Eph, Phe	Bolus	NP	SBP <90	2
16	9	Frey et al., a) 2018[64]	19	Ringer lactate group	Coloading effects on hemodynamics	52 ± 16.5	NP	70°	Shoulder surgery	NP	GA ± ISB	I-II	Propofol	Propofol, Sufentanil, cisatracurium	NP	NP	Coloading with ringer lactate, NE	Nil	Nil	Nil	0 (0%)	NE	Bolus and infusioin	8.9 ± 7.4 μg/min[a]	MAP <80 or >20% decrease from BL	5
17	9	Frey et al., b) 2018[64]	20	HES 130/0.4 group		56 ± 15.6	NP	70°	Shoulder surgery	NP	GA ± ISB	I-II	Propofol	Propofol, Sufentanil, Cisatracurium	NP	NP	Coloading HES, NE	Nil	Nil	Nil	0 (0%)	NE	Bolus and infusioin	10.4 ± 7.9 μg/min[a]	MAP <80 or >20% decrease from BL	5
18	10	Hanouz et al., 2016[54]	53	Study	MCA blood flow velocity in BCP	49 ± 20	90 (58-120)	NP	Shoulder surgery	18/2/9	GA + ISB	I-III	Propofol	Sufentanil, sevoflurane or desflurane	NP	0.33% ropivacaine, 15-20ml	Nil	Nil	Nil	Nil	29 (55%)	Eph, Phe	Bolus	Eph, 15 (9-21)mg; phe, 225 (75-550)μg[a]	NP	-1
19	11	Hasanein et al., a) 2014[28]	49	Group I (ondansetron, 4 mg)	Effect of ondansetron in preventing HBE	46.7 ± 3.3	NP	60-80°	Shoulder arthroscopy	NP	ISB + sedation	I-II	NA	NA	USG + PNS	0.5% bupivacaine	Nil	3 (6.1%)	1	Atropine	3	Eph	Bolus	n= 3	Liguori et al.[$]	4
20	11	Hasanein et al., b) 2014[28]	50	Group II (ondansetron, 8 mg)		48.1 ± 4.2	NP	60-80°	Shoulder arthroscopy	NP	ISB + sedation	I-II	NA	NA	USG + PNS	0.5% bupivacaine	Nil	3 (6%)	2 (4%)	Atropine	3 (6%)	Eph	Bolus	n= 3	Liguori et al.[$]	4
21	11	Hasanein et al., c) 2014[28]	49	Group III (Control)		47 ± 2.1	NP	60-80°	Shoulder arthroscopy	NP	ISB + sedation	I-II	NA	NA	USG + PNS	0.5% bupivacaine	Nil	10 (20.4%)	5 (10.2%)	Atropine	10 (20.4%)	Eph	Bolus	n= 10	Liguori et al.[$]	4
22	12	Jang et al., a) 2016[29]	25	Control	Effect of dexmedetomidine on S-100 β levels	61.2 ± 8.2	103.2 ± 20.4	80°	Shoulder arthroscopy	NP	GA + ISB	NP	Propofol, Remifentanil	Sevoflurane	USG	0.75% ropivacaine, 10ml	NP	12 (48%)	1 (4%)	Atropine, 0.5mg	11 (44%)	Phe, Eph	Bolus	n = 11	SBP <90 or >20% decrease from BL	5
23	12	Jang et al., b) 2016[29]	25	Study		58.1 ± 7.6	100.8 ± 20.7	80°	Shoulder arthroscopy	NP	GA + ISB	NP	Propofol, Remifentanil	Sevoflurane	USG	0.75% ropivacaine, 9ml and dexmedetomidine 100μg	NP	25 (100%)	2 (8%)	Atropine, 0.5mg	23 (92%)	Phe, Eph	Bolus and AVP loading dose	n = 23	SBP <90 or >20% decrease from BL	5
24	13	Jang et al., a) 2017[35]	15	PR-Saline	Effects of anaesthetics and AVP on Hemodynamics and cerebral oxygenation	62 (46-70)	151 ± 45	65-75°	Shoulder surgery	5/4/NP	GA, TIVA Propofol	I-III	Propofol, Remifentanil	Propofol, Remifentanil	Nil	Nil	Nil	Nil	Nil	Nil	11 (73%)	Eph	Bolus	n = 11, 15 ± 4mg[a]	MAP <50	2
25	13	Jang et al., b) 2017[35]	15	PR-AVP		59 (53-78)	161 ± 29	65-75°	Shoulder surgery	7/1/NP	GA, TIVA Propofol	I-III	Propofol, Remifentanil	Propofol, Remifentanil	Nil	Nil	AVP, 0.05 U/kg bolus	Nil	Nil	Nil	4/16 (25%)	Eph	Bolus and AVP loading dose	n = 4, 10 ± 4mg[a]	MAP <50	2
26	13	Jang et al., c) 2017[35]	15	SN-Saline		62 (45-77)	181 ± 56	65-75°	Shoulder surgery	4/2/NP	GA	I-III	Propofol, Remifentanil	N_2O, sevoflurane	Nil	Nil	Nil	Nil	Nil	Nil	6 (40%)	Eph	Bolus	n = 6, 13 ± 4mg[a]	MAP <50	2
27	13	Jang et al., d) 2017[35]	15	SN-AVP		65 (51-73)	173 ± 34	65-75°	Shoulder surgery	5/2/NP	GA	I-III	Propofol, Remifentanil	N_2O, sevoflurane	Nil	Nil	AVP, 0.05 U/kg bolus	Nil	Nil	Nil	3 (20%)	Eph	Bolus	n = 3, 11 ± 5mg[a]	MAP <50	2
28	14	Jansen et al., a) 2014[30]	42	GA	BP response to GA or GA + ISB for shoulder arthroscopy	51 ± 10	56.0 ± 12.4	NP	Shoulder arthroscopy	NP/NP/beta blockers, n=7	TIVA Propofol	I-II	Propofol, Remifentanil or Sufentanil	Propofol, Remifentanil, and/or Sufentanil	Nil	Nil	Nil	Nil	8 (19%)	Atropine	27 (64%)	Cafedrine, Theoadrenaline	Bolus	NP	MAP <60 or SBP >20% decrease from BL	5
29	14	Jansen et al., b) 2014[30]	41	GA + ISB		53 ± 9	46.0 ± 15.3	NP	Shoulder arthroscopy	NP/NP/ beta blockers, n=5	GA, TIVA Propofol	I-II	Propofol, Remifentanil or Sufentanil	Propofol, Remifentanil, and/or Sufentanil	PNS	1% mepivacaine, 40ml	Nil	Nil	5 (12.2%)	Atropine	31 (76%)	Cefedrine, Theoadrenaline	Bolus	NP	MAP <60 or SBP >20% decrease from BL	5
30	15	Jeong et al., a) 2012[16]	19	SN	Anaesthetic influences on cerebral oxygen saturation	65 ± 9	193 ± 63	65-75°	Shoulder arthroscopy	6/2/beta blockers, n=5	GA	I-III	Propofol, Remifentanil	N_2O, sevoflurane	Nil	Nil	Nil	Nil	Nil	Nil	7 (36%)	Eph	Bolus	14 ± 4mg[a]	MBP <50	4
31	15	Jeong et al., b) 2012[16]	17	PR		60 ± 7	188 ± 58	65-75°	Shoulder arthroscopy	4/4/beta blockers, n=2	GA, TIVA Propofol	I-III	Propofol, Remifentanil	Propofol, Remifentanil	Nil	Nil	Nil	Nil	Nil	Nil	3/20 (15%)	Eph	Bolus	13 ± 5mg[a]	MBP <50	4
32	16	Jo et al., a) 2013[55]	20	Control	Effect of warmed inspired gas on body temperature	47.5 ± 16.6	125 ± 48	70°	Shoulder arthroscopy	5/1/NP	GA	I-II	Propofol	Sevoflurane	Nil	Nil	Nil	Nil	Nil	Nil	6 (30%)	Eph, Phe	Bolus	NP	MBP <60 or <80% of BL	2
33	16	Jo et al., b) 2013[55]	20	Heated		50.4 ± 14.1	129 ± 50	70°	Shoulder arthroscopy	7/1/NP	GA	I-II	Propofol	Sevoflurane	Nil	Nil	Nil	Nil	Nil	Nil	5 (25%)	Eph, Phe	Bolus	NP	MBP <60 or <80% of BL	2
34	17	Jo et al., a) 2014[40]	25	Study, non-hypotension	Prediction of hypotension based on pre-operative variables	42 ± 5	NP	70°	Shoulder arthroscopy	0/NP/NP	GA	I-II	Propofol, alfentanyl	Sevoflurane	Nil	Nil	SCD	Nil	Nil	Nil	0 (0%)	Eph, Phe	Bolus	n = 0	MBP <60 or >20% decrease from BL	-1
35	17	Jo et al., b) 2014[40]	15	Study, hypotension		50 ± 6	NP	70°	Shoulder arthroscopy	0/NP/NP	GA	I-II	Propofol, alfentanyl	Sevoflurane	Nil	Nil	SCD	Nil	Nil	Nil	15 (100%)	Eph, Phe	Bolus	Eph, 5 (5-10)mg, Phe, 100 (20-200)μg[a]	MBP <60 or >20% decrease from BL	-1
36	18	Jung et al., a) 2007[41]	20	Sevoflurane	Cardivascular effects by sevoflurane vs *Propofol*	44.1 ± 15.2	NP	70°	Shoulder arthroscopy	NP	GA	I-II	Thiopentone	Sevoflurane, alfentanyl	Nil	Nil	Compression stockings	Nil	Nil	Nil	2 (10%)	Phe, Eph	Bolus	Eph, n = 2; Phe, n = 1	MBP <60	0
37	18	Jung et al., b) 2007[41]	20	Propofol		45.6 ± 14.1	NP	70°	Shoulder arthroscopy	NP	GA	I-II	Propofol	TCI Propofol	Nil	Nil	Compression stockings	Nil	Nil	Nil	3 (15%)	Phe, Eph	Bolus	Eph, n = 1; Phe, n = 2	MBP <60	0
38	19	Kim et al., a) 2009[42]	17	Control	Effect of SCD on BCP hypotension	43.7 ± 11.2	NP	70°	Shoulder arthroscopy	0/0/0	GA	I	Propofol, Remifentanil	Sevoflurane, Remifentanil	Nil	Nil	Nil	Nil	Nil	Nil	12 (70.6%)	Phe, Eph	Bolus	Eph, 0 (0-5)mg, Phe, 50 (0-100)μg[a]	MBP <60 or >20% decrease from BL	5
39	19	Kim et al., b) 2009[42]	16	SCD		37.5 ± 12.4	NP	70°	Shoulder arthroscopy	0/0/1	GA	I	Propofol, Remifentanil	Sevoflurane, Remifentanil	Nil	Nil	SCD	Nil	Nil	Nil	5 (31.3%)	Phe, Eph	Bolus	Eph, 0 (0-0)mg, Phe, 0 (0-75)μg[a]	MBP <60 or >20% decrease from BL	5
40	19	Kim et al., c) 2009[42]	15	ES		41.2 ± 12.8	NP	70°	Shoulder arthroscopy	0/0/2	GA	I	Propofol, Remifentanil	Sevoflurane, Remifentanil	Nil	Nil	ES	Nil	Nil	Nil	7 (46.7%)	Phe, Eph	Bolus	Eph, 0 (0-5)mg, Phe, 0 (0-50)μg[a]	MBP <60 or >20% decrease from BL	5
41	20	Kim et al., 2015[31]	64	Study	HR variability after ISB in BCP	48.8 ± 12.2[d]	110.1 ± 32.9[d]	70-80°	Shoulder arthroscopy	NP	ISB ± sedation	I-II	NA	NA	PNS	1% mepivacaine, 20ml, 0.75% ropivacaine, 20ml	Plasmalyte infusion	18 (28.1%)	NP	Atropine	NP	Eph, E	Bolus	NP	Liguori et al.[$]	-1
42	21	Kocaoglu et al., 2014[43]	53	Study	Cerebral Oxymetry values for prediction of cerebral ischaemia	58 (42-68)	NP	NP	Shoulder arthroscopy	NP	GA	I-II	Propofol	Remifentanil, N_2O, sevoflurane	Nil	Nil	Nil	Nil	Nil	Nil	NP	E	Bolus	NP	MBP <60	-1
43	22	Koh et al., a) 2013[56]	30	GA	Comparitive effects of GA vs *ISB on cerebral oxygenation*	50.4 ± 16.5	NP	70°	Shoulder arthroscopy	9/2/10	GA	I-III	Propofol, lignocaine	Sevoflurane	USG or PNS	Ropivacaine	Nil	Nil	Nil	Nil	22 (73.3%)	Phe	Bolus	400 (0-1840)mg, n = 31	MBP >20% decrease from BL	-1
44	22	Koh et al., b) 2013[56]	30	ISB		55.5 ± 13.3	NP	70°	Shoulder arthroscopy	7/7/11	ISB + sedation	I-III	NA	Propofol sedation	USG or PNS	Ropivacaine	Nil	Nil	Nil	Nil	3 (10%)	Phe	Bolus	0 (0-560), n = 9	MBP >20% decrease from BL	-1
45	23	Kwak et al., a) 2010[44]	25	Control	Effect of SCD on hemodynamics	47 ± 10	NP	70°	Shoulder arthroscopy	0/0/NP	GA	I-II	Propofol, Remifentanil	Sevoflurane, Remifentanil	Nil	Nil	6% HES preload	Nil	Nil	Nil	16 (64%)	Eph	Bolus	0 (0-10)mg[a]	MBP <60 or >20% decrease from BL	4
46	23	Kwak et al., a) 2010[44]	25	SCD		43 ± 16	NP	70°	Shoulder arthroscopy	0/0/NP	GA	I-II	Propofol, Remifentanil	Sevoflurane, Remifentanil	Nil	Nil	6% HES preload	Nil	Nil	Nil	7 (28%)	Eph	Bolus	5 (0-6.25)mg[a]	MBP <60 or >20% decrease from BL	4
47	24	Kwak et al., a) 2011[45]	33	control	Effect of SCD on cerebral oxygenation	46 ± 12	NP	70°	Shoulder arthroscopy	0/0/NP	GA	I-II	Propofol, Remifentanil	Sevoflurane, Remifentanil	Nil	Nil	6% HES preload	Nil	Nil	Nil	8 (24.2%)	Eph	Bolus	n = 8, 36mg	MBP <60 or >20% decrease from BL	4
48	24	Kwak et al., b) 2011[45]	33	SCD		42 ± 12	NP	70°	Shoulder arthroscopy	0/0/NP	GA	I-II	Propofol, Remifentanil	Sevoflurane, Remifentanil	Nil	Nil	6% HES preload	Nil	Nil	Nil	1 (3.03%)	Eph	Bolus	n = 1, 4mg	MBP <60 or >20% decrease from BL	4
49	25	Kwak et al., a) 2017[46]	20	Normocapnoea	Hypercapnea effect on lung oxygenation	53 ± 8	NP	70°	Shoulder arthroscopy	NP	GA	I-II	Propofol, alfentanyl	Sevoflurane	Nil	Nil	6% HES preload	Nil	Nil	Nil	9 (45%)	Phe, Eph	Bolus	Eph, n = 2; Phe, n = 6	MBP <60	2
50	25	Kwak et al., b) 2017[46]	20	Hypercapnoea		50 ± 9	NP	70°	Shoulder arthroscopy	NP	GA	I-II	Propofol, alfentanyl	Sevoflurane	Nil	Nil	6% HES preload	Nil	Nil	Nil	7 (35%)	Phe, Eph	Bolus	Eph, n = 4; Phe, n = 7	MBP <60	2
51	26	Larsen et al., 2014[36]	14	Reclining BCP	CVS effects of induction positions for BCP surgeries	42 ± 15	NP	60°	Shoulder arthroscopy	NP	GA + ISB	I-II	Propofol, Remifentanil	Propofol, Remifentanil	NP	0.75% ropivacaine, 10-20ml	Compression stocking devices	Nil	Nil	Nil	5 (35.7%)	Eph	Bolus	4mg[f]	MBP <60	-1
52	27	Lee et al., 2014[57]	30	Study	Effect of BCP on BIS	48 ± 9.8	NP	70°	Shoulder arthroscopy	0/NP/NP	GA	I-II	Thiopentone,fentanyl	N_2O, sevoflurane	Nil	Nil	6% HES preload	Nil	Nil	Nil	NP	NP	NP	NP	MBP <60	-2
53	28	Lee et al., 2015[58]	40	Study	Prediction of fluid responsiveness in BCP	62 ± 9.7[d]	147.9 ± 21.7[d]	70°	Shoulder arthroscopy	16/7/NP	GA	I-III	Propofol, Remifentanil	Sevoflurane	Nil	Nil	Nil	Nil	Nil	Nil	7 (17.5%)	Eph	Bolus	NP	MBP <60	-1
54	29	Liguori et al., a) 1998[26]	47	Placebo	Role of metoprolol and glycopyrrolate in prevention of HBE	38 ± 13	NP	60-80°	Shoulder arthroscopy	NP	ISB + sedation	I-II	NA	NA	Paresthesia	1.5% mepivacaine, 10 mg/kg, E, 1:200000	Nil	13 (27.7%)	Nil	Atropine	NP	Eph, E	Bolus	NP	Liguori et al.[$]	3
55	29	Liguori et al., b) 1998[26]	56	Metoprolol		42 ± 12	NP	60-80°	Shoulder arthroscopy	NP	ISB + sedation	I-II	NA	NA	Paresthesia	1.5% mepivacaine, 10 mg/kg, E, 1:200000	Nil	3 (5.4%)	Nil	Atropine	NP	Eph, E	Bolus	NP	Liguori et al.[$]	3
56	29	Liguori et al., c) 1998[26]	46	Glycopyrrolate		42 ± 11	NP	60-80°	Shoulder arthroscopy	NP	ISB + sedation	I-II	NA	NA	Paresthesia	1.5% mepivacaine, 10 mg/kg, E, 1:200000	Nil	10 (21.8%)	Nil	Atropine	NP	Eph, E	Bolus	NP	Liguori et al.[$]	3
57	30	Maghawry et al., a) 2015[47]	25	Dexmedetomidine	Dexmed vs Esmolol effects on rSO_2	41.1 ± 10.3	160.4 ± 11.2	65-75°	Shoulder arthroscopy	NP	GA	I-II	Propofol, fentanyl	N_2O, sevoflurane	Nil	Nil	Nil	NP	Nil	NP	NP	NP	NP	NP	MBP <50	5
58	30	Maghawry et al., b) 2015[47]	25	Esmolol		36.9 ± 12	155.4 ± 14.1	65-75°	Shoulder arthroscopy	NP	GA	I-II	Propofol, fentanyl	N_2O, sevoflurane	Nil	Nil	Nil	NP	Nil	NP	NP	NP	NP	NP	MBP <50	5
59	31	McCulloh et al., 2010[66]	19	Study	MCA blood flow velocity in BCP	68 ± 7	NP	45°	Shoulder arthroscopy	12/4/8	GA	III	Propofol	Desflurane	Nil	Nil	Nil	NP	Nil	NP	11 (57.9%)	Phe	Infusion	NP	MBP <50	-1
60	32	Meex et al., 2016[59]	101	Study	Cerebral oxygenation in BCP	53 (13)	NP	NP	Shoulder arthroscopy	14/NP/NP	GA + ISB	III	Propofol, Remifentanil	Propofol, Remifentanil	NP	0.5% bupivacaine, 30ml	Nil	Nil	Nil	Nil	NP	Phe, Eph	Bolus	NP	MBP <60	-1
61	33	Mori et al., a) 2015[48]	28	Healthy controls	Cerebral oxygenation in BCP in patients with CVS risk factors	55 ± 16	NP	60°	Shoulder arthroscopy	0/0/0	GA	I	Propofol	Sevoflurane	Nil	Nil	Nil	Nil	Nil	Nil	NP	Eph, Phe	Bolus	Eph, 0.86 ± 3.3mg[a]; Phe, 0.13 ± 0.2mg[a]	MBP <60	-1
62	33	Mori et al., b) 2015[48]	33	Study, 1 risk factor		59 ± 14	NP	60°	Shoulder arthroscopy	9/5/1	GA	I-II	Propofol	Sevoflurane	Nil	Nil	Nil	Nil	Nil	Nil	NP	Eph, Phe	Bolus	Eph, 0.73 ± 2.5mg[a]; Phe, 0.22 ± 0.38mg[a]	MBP <60	-1
63	33	Mori et al., c) 2015[48]	30	Study, 2 risk factors		65 ± 10	NP	60°	Shoulder arthroscopy	22/14/7	GA	I-III	Propofol	Sevoflurane	Nil	Nil	Nil	Nil	Nil	Nil	NP	Eph, Phe	Bolus	Eph, 4.4 ± 9.0mg[a]; Phe, 0.48 ± 0.48mg[a]	MBP <60	-1
64	34	Murphy et al., a) 2014[60]	34	study	Effect of ventilation on cereberal oxygenation	54.7 ± 12.4	98 (75-185)	80-90°	Shoulder arthroscopy	12/5/9	GA	I-III	Propofol, fentanyl	Sevoflurane, fentanyl	Nil	Nil	Nil	Nil	Nil	Nil	34 (100%)	Phe	Bolus	240 (0-2880)μg[a]	MBP >20% decrease from BL	4
65	34	Murphy et al., b) 2014[60]	36	Control		52.3 ± 13.8	96 (40-193)	80-90°	Shoulder arthroscopy	15/5/8	GA	I-III	Propofol, fentanyl	Sevoflurane, fentanyl	Nil	Nil	Nil	Nil	Nil	Nil	36 (100%)	Phe	Bolus	320 (0-1500)μg[a]	MBP >20% decrease from BL	4
66	35	Murphy et al., 2010[65]	61	Study	Cerebral desaturation in BCP	49.8 ± 13.9	117 ± 31	80-90°	Shoulder arthroscopy	26/3/20	GA ± ISB	I-III	Propofol, fentanyl	Sevoflurane, fentanyl	NP	NP	Nil	Nil	Nil	Nil	46 (76%)	Eph, Phe	Bolus	1 (0-6)[f]	MBP >20% decrease from BL	-1
67	36	Nallam et al., 2015[13]	49	Control	Effect of ondansetron in preventing HBE	33.9 ± 9.4	103 ± 38	60-80°	Shoulder arthroscopy	0/0/NP	ISB + sedation	I-II	NA	NA	PNS	0.5% levobupivacaine, 35ml	Crystalloid preloading, 500ml	11 (22.4%)	5 (10.2%)	Atropine, 0.6mg	9 (18.4%)	Eph	Bolus	NP	Liguori et al.[$]	2
68	36	Nallam et al., 2015[13]	49	Study		34.3 ± 8.8	109 ± 31	60-80°	Shoulder arthroscopy	0/0/NP	ISB + sedation	I-II	NA	NA	PNS	0.5% levobupivacaine, 35ml	Crystalloid preloading, 500ml	3 (6.1%)	1 (2.04%)	Atropine, 0.6mg	3 (6.1%)	Eph	Bolus	NP	Liguori et al.[$]	2
69	37	Oh et al., 2019[27]	34	Control	Effect of Remote Ischemic Preconditioning on Cerebral oxygenation	60 (12)	166 (48)	NP	Shoulder surgery	11/6/NP	GA	NP	Thiopentone, Remifentanil	Sevoflurane, Remifentanil	Nil	Nil	Nil	NP	9 (26.5%)	Atropine, 0.5mg	Unclear	Phe, Eph	Bolus	Phe, 678 (1665); Eph, 0 (0)	MAP < 65	5
70	37	Oh et al., 2019[27]	29	Study		60 (16)	177 (48)	NP	Shoulder surgery	8/1/NP	GA	NP	Thiopentone, Remifentanil	Sevoflurane, Remifentanil	Nil	Nil	Remote ischemic preconditioning	NP	5 (17.4%)	Atropine, 0.5mg	Unclear	Phe, Eph	Bolus	Phe, 120 (1465); Eph, 0 (0)	MAP < 66	5
71	38	Ozturk et al., a) 2015[49]	20	Levobupivacaine	Desflurane consumption in BCP surgeries in patients recieving LAs.	48.1±11.4	123.5 ± 50.4	NP	Shoulder arthroscopy	NP	GA + ISB	I-II	Thiopentone, Remifentanil	Desflurane, N_2O	PNS	0.25% levobupivacaine, 40ml	Nil	Nil	Nil	Nil	NP	Eph	Bolus	NP	NP	5
72	38	Ozturk et al., b) 2015[49]	20	Bupivacaine		45.8±13.3	88.8 ± 36.3	NP	Shoulder arthroscopy	NP	GA + ISB	I-II	Thiopentone, Remifentanil	Desflurane, N_2O	PNS	0.25% bupivacaine, 40ml	Nil	Nil	Nil	Nil	NP	Eph	Bolus	NP	NP	5
73	38	Ozturk et al., c) 2015[49]	20	Control		39.2±14.5	106.1 ± 51.5	NP	Shoulder arthroscopy	NP	GA	I-II	Thiopentone, Remifentanil	Desflurane, N_2O	Nil	Nil	Nil	Nil	Nil	Nil	NP	Eph	Bolus	NP	NP	5
74	39	Picton et al., a) 2015[61]	29	Propofol	Influence of ventilation and anesthesia on cerebral oxymetry	51.3 ± 10.0	NP	80-90°	Shoulder arthroscopy	0/1/8	GA + ISB	I-III	Propofol, fentanyl	Propofol	USG	0.5% ropivicaine, 20ml	Nil	Nil	Nil	Nil	13 (44.8 %)	Eph, Phe	Bolus	Eph, 70mg, n = 8; phe, 1000μg, n = 5	MBP >20% decrease from BL	5
75	39	Picton et al., b) 2015[61]	27	Desflurane		49.3 ± 13.3	NP	80-90°	Shoulder arthroscopy	0/0/5	GA + ISB	I-III	Propofol, fentanyl	Desflurane	USG	0.5% ropivicaine, 20ml	Nil	Nil	Nil	Nil	17 (62.9%)	Eph, Phe	Bolus	Eph, 90mg, n = 10; phe, 1800μg, n = 7	MBP >20% decrease from BL	5
76	40	Schotola et al., a) 2015[37]	150	Control	Effect of ketamine in shoulder arthroscopy hemodynamics	50 ± 11	80 ± 28	NP	Shoulder arthroscopy	NP	GA	I-III	Propofol, Remifentanil	Propofol, Remifentanil	Nil	Nil	Nil	Nil	Nil	Nil	96 (64%)	Theoadrenaline + cafedrine	Bolus	1.4 ± 0.9ml[a]	MBP >20% decrease from BL	3
77	40	Schotola et al., b) 2015[37]	150	Ketamine		52 ±11	92 ±30	NP	Shoulder arthroscopy	NP	GA	I-III	Propofol, fentanyl	Propofol, Remifentanil, ketamine	Nil	Nil	Nil	Nil	Nil	Nil	99 (66%)	Theoadrenaline + cafedrine	Bolus	1.3 ± 0.8ml[a]	MBP >20% decrease from BL	3
78	41	Sia et al., a) 2003[4]	55	Plain	Effects of epinephrine on incidence of HBE	54 ± 11	NP	60-80°	Shoulder surgery	NP	ISB + sedation	I-II	NA	NA	PNS	0.5% bupivacaine, 2% lidocaine; 35ml	NP	6 (11%)	NP	Atropine	17 (30.9%)	Eph	Bolus	NP	Liguori et al.[$]	2
79	41	Sia et al., b) 2004[4]	55	E		58 ± 15	NP	60-80°	Shoulder surgery	NP	ISB + sedation	I-II	NA	NA	PNS	0.5% bupivacaine, 2% lidocaine, 1:200000 adrenaline; 35ml	NP	16 (29%)	NP	Atropine	2 (3.63%)	Eph	Bolus	NP	Liguori et al.[$]	2
80	42	Soeding et al., a) 2011[50]	20	GA	Effect of BCP on CBF	50 ± 13	43 ± 13	75-80°	Shoulder arthroscopy	NP	GA	I-II	Propofol, fentanyl	Sevoflurane	USG	0.75% ropivacaine, 3mg/kg	Prehydration 15ml/kg NS	Nil	Nil	Nil	17 (85%)	Metaraminol	Bolus	NP	MBP <65	2
81	42	Soeding et al., b) 2011[50]	20	Sedation		48 ± 11	42 ± 13	75-80°	Shoulder arthroscopy	NP	ISB ± sedation	I-II	NA	NA	USG	0.75% ropivacaine, 3mg/kg	Prehydration 15ml/kg NS	Nil	Nil	Nil	2 (10%)	Metaraminol	Bolus	NP	MBP <65	2
82	43	Soeding et al., a) 2013[15]	17	Saline	Effect of phenylephrine on cerebral oxygen saturation	40 (32-48)	NP	>75°	Shoulder surgery	NP	GA + ISB	I-II	Propofol, fentanyl	Sevoflurane	USG	0.75% ropivacaine, 30-35ml	Prehydration with Hartmann solution	Unclear	Nil	Nil	4 (25%)	Metaraminol	Bolus	NP	MBP <65	2
83	43	Soeding et al., b) 2013[15]	17	Phe		47 (37-57)	NP	>75°	Shoulder surgery	NP	GA + ISB	I-II	Propofol, fentanyl	Sevoflurane	USG	0.75% ropivacaine, 30-35ml	Prehydration with Hartmann solution, Phe infusion	Unclear	Unclear	Unclear	2 (11%)	Metaraminol	Bolus	NP	MBP <65	2
84	44	Song et al., a) 2011[12]	40	Saline	Effect of fentanyl on HBE	48.1 ± 2.5	149.7 ± 7.2	60-80°	Shoulder arthroscopy	NP	ISB + sedation	I-II	NA	NA	PNS	0.75% bupivacaine, 1% lidocaine or mepivacaine, 40 ml	NP	4 (10%)	0 (0%)	Atropine	4 (10%)	Eph	Bolus	NP	HR <50 and/or SBP <100	2
85	44	Song et al., b) 2011[12]	40	Fentanyl-50		47.4 ± 2.7	140.1 ± 10.7	60-80°	Shoulder arthroscopy	NP	ISB + sedation	I-II	NA	NA	PNS	0.75% bupivacaine, 1% lidocaine or mepivacaine, 40 ml	NP	6 (15%)	5 (12.5%)	Atropine	6 (15%)	Eph	Bolus	NP	HR <50 and/or SBP <100	2
86	44	Song et al., c) 2011[12]	40	Fentanyl-100		47.5 ± 2.6	142.4 ± 10.7	60-80°	Shoulder arthroscopy	NP	ISB + sedation	I-II	NA	NA	PNS	0.75% bupivacaine, 1% lidocaine or mepivacaine, 40 ml	NP	11 (27.5%)	3 (7.5%)	Atropine	11 (27.5%)	Eph	Bolus	NP	HR <50 and/or SBP <100	2
87	44	Song et al., d) 2011[12]	40	Ketorolac-30		51.8 ± 2.3	163.7 ± 9.7	60-80°	Shoulder arthroscopy	NP	ISB + sedation	I-II	NA	NA	PNS	0.75% bupivacaine, 1% lidocaine or mepivacaine, 40 ml	NP	2 (5%)	0 (0%)	Atropine	2 (5%)	Eph	Bolus	NP	HR <50 and/or SBP <100	2
88	45	Tange et al., 2010[62]	30	Study and control	Cerebral oxygenation in BCP under GA	55 ± 13	NP	60°	Shoulder surgery	8/6/NP	GA	NP	Propofol, butorphanol	Sevoflurane	Nil	Nil	Supportive stockings	Nil	Nil	Nil	NP	Phe	Bolus	0.04 ± 0.07mg[a]	MBP <60	-1
89	46	Vincent et al., 2005[32]	140	Study	TCI seadation for BCP arthroscopy	50.8 ± 13.7	72.1 ± 27	NP	Shoulder arthroscopy	92/44/4	ISB + sedation	I-III	NA	NA	PNS	0.75% ropivacaine, 30ml	Prehydration 10ml/kg RL	8 (5.7%)	NP	Atropine	NP	Eph	Bolus	5.6 ± 4.1mg[a]	Liguori et al.[$]	-1
90	47	Zhu et al., a) 2014[63]	17	Control	BCP induced plethysmographic waveform analysis	NP	NP	>60°	Shoulder surgery	NP	GA + ISB	I-III	Propofol, fentanyl	Sevoflurane	USG	0.5% bupivacaine	Nil	Nil	Nil	Nil	0 (0%)	NA	Bolus	NA	MBP <65 or >20% decrease from BL	-1
91	47	Zhu et al., b) 2014[63]	12	Phe		NP	NP	>60°	Shoulder surgery	NP	GA + ISB	I-III	Propofol, fentanyl	Sevoflurane	USG	0.5% bupivacaine	Nil	Nil	Nil	Nil	12 (100%)	Eph, Phe	Bolus	NP	MBP <65 or >20% decrease from BL	-1

Supplementary Digital Content File 3: Characteristics of included study groups. ASA PS - American Society of Anaesthesiologists Physical Status; AVP - Arginine vasopressin; BCP - Beach chair position; BIS - Bispectral index; BL - Baseline; BP - Blood pressure; CVS - Cardiovascular system; CBF - Cerebral blood flow; DM - Diabetes mellitus; E - Epinephrine; Eph - Ephedrine; ES - Elastic stockings; GA - General anaesthesia; HBE - Hypotension bradycardia episode; HES - Hydroxyethyl starch; HR - Heart rate; HTN - hypertension; IOP - Intraocular pressure; ISB - Interscalene block; LA - Local anaesthetics; MAP - Mean arterial pressure; MBP - Mean blood pressure; MCA - Middle cerebral artery; N_2O - Nitrous oxide; NA - not applicable; NE - Norepinephrine; NIRS - Near infra-red spectroscopy; NP - Not provided; NS - Normal saline; O_2 - Oxygen; Phe - Phenylephrine; PNS - Peripheral nerve stimulator; PR - Propofol remifentanil; RL - Ringer lactate; SBP - Systolic blood pressure; SCD - Sequential compression device; SN - Sevoflurane nitrous oxide; SG - Study group; TCI - Target controlled infusion; TIVA - Total intravenous anaesthesia; USG - Ultrasound guided. *per subject; ^average incidence per subject in a SG. [$]Liguori *et al.*, defined HBE as HR <50 beats/min at anytime or <30 beats in less than 5 minute compared to pre-anaesthetic state with or without hypotension, and/or decrease in SBP >30 mmHg in <5 min compared to pre-anaesthetic values, or any SBP decrease <90 mm Hg; necessarily treated by ephedrine, epinephrine or atropine. **pooled data. [#]only mean value is provided. [¯]interventions per subject

Note (Supplementary Digital Content File 3):

Analysis details: Data of studies which include both analysis; (1) HR data of adverse HR-responses (first analysis); (2) HR data of HR-variability (second analysis). To define an 'adverse event', authors' own definitions have been used. Details of bradycardia/HBE or hypotension are shown in separate columns.

During second analysis of HR variabilities, we found no publication bias for EHR and DHR (Egger's test, $P = 0.836$ and 0.976, respectively) for included studies. However, funnel plot showed that the study by Meex *et al.*,[59] influenced the analysis (Egger's test, $P < 0.001$). Excluding this study resulted in non-significant P value ($P = 0.06$) for MHR responses. However, inclusion of this study did not alter the overall outcomes for MHRs. Please see Supplementary Digital Content File 5 for 'Publication bias'.

Use of prophylactic vasopressor infusions (PVIs) and effect on HR, rSO_2 and HR-rSO_2 relationships: PVIs were used in 10 SGs. The certainty of the effects of PVIs on HR necessitated additional analyses on the control groups of each trial. Meta-analysis clearly demonstrated lower HR in BCP among SGs using PVIs as compared to those not using them ($P = 0.004$, within trials).[15,33-35] When SGs using PVIs were compared in pre- and post-BCP, lower HRs were not observed ($P = 0.23$, within SGs).[15,33-35] The overall association of PVIs vis-à-vis HR changes in BCP was non-significant (sensitivity analysis and meta-regression). Since we considered rSO_2 values for the entire duration of surgery, no attempt was made to establish relationships between the two. Further, meta-correlation analyses were considered on HR-rSO_2 relationships with and without use of PVIs. The use of PVIs did not make a difference (with PVIs use, $r = 0.693$, 95%CI, 0.391 to 0.860, $P < 0.001$, random effects, $I^2 = 72.5\%$, $n = 90$ and without PVIs use, $r = 0.560$, 95%CI, 0.332 to 0.727, $P < 0.001$, random effects, $I^2 = 80.81\%$, $n = 291$).

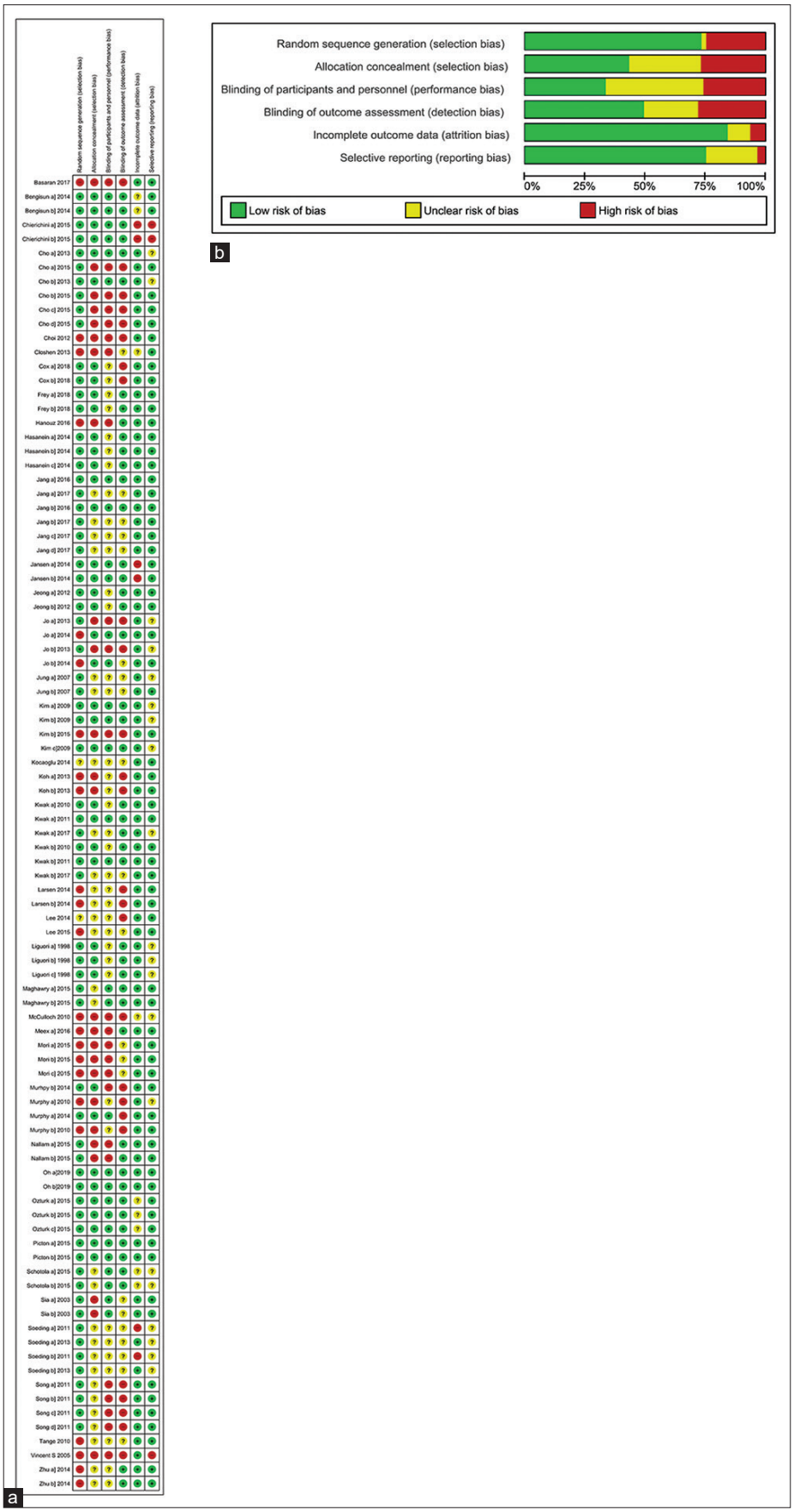
Relationship between rSO_2 and MBP: Twenty SGs[16,33-35,46,56,60,65] evaluated MBP and rSO_2 at specific intervals over the entire BCP period. Data were recorded as statistical averages for absolute values of consecutive timings. Meta-correlation analysis showed statistically significant correlation between MBP and rSO_2 values ($r = 0.597$, 95% CI, 0.432 to 0.723, $P < 0.001$, random effects, $I^2 = 79.9\%$) confirming the predictable relationship between the two.

Physiological controls and HR: Four SGs[31,53,59,62] evaluated HR responses over time. Meta-analysis demonstrated no change of HR after positioning to BCP ($P = 0.58$).

Vaso-active drugs consumption: Pooled averages of ephedrine requirements (mgs) were higher for GA ± ISB ($n = 83$) subjects[54,56] than GA alone[16,33,35,40,44,48,60,62] ($n = 390$) to maintain the desired BP (23.1 ± 32.1 *vs* 15.4 ± 27.3, per subject, respectively, $P = 0.026$). Ephedrine consumptions in inhalation anaesthesia[16,35,40,44,48,54,56,60] ($n = 396$) and TIVA-propofol[16,33,35] ($n = 77$) were 17.8 ± 31.1 and 12.4 ± 5.9 respectively ($P = 0.236$). CDEs, rSO_2 and HR measurements were not analysed for vaso-active drug consumptions as the timings of administration were inadequately available.

Jadad scores: Variable Jadad scores (-2 to 5) were observed for included studies as inclusion of studies to this meta-analysis was not set for minimum scores. Inclusion of all studies would not change the incidences of adverse HR-responses. This is because all subjects of BCP-surgery were analysed pre– and post-BCP status in addition to comparative controls during analysis.

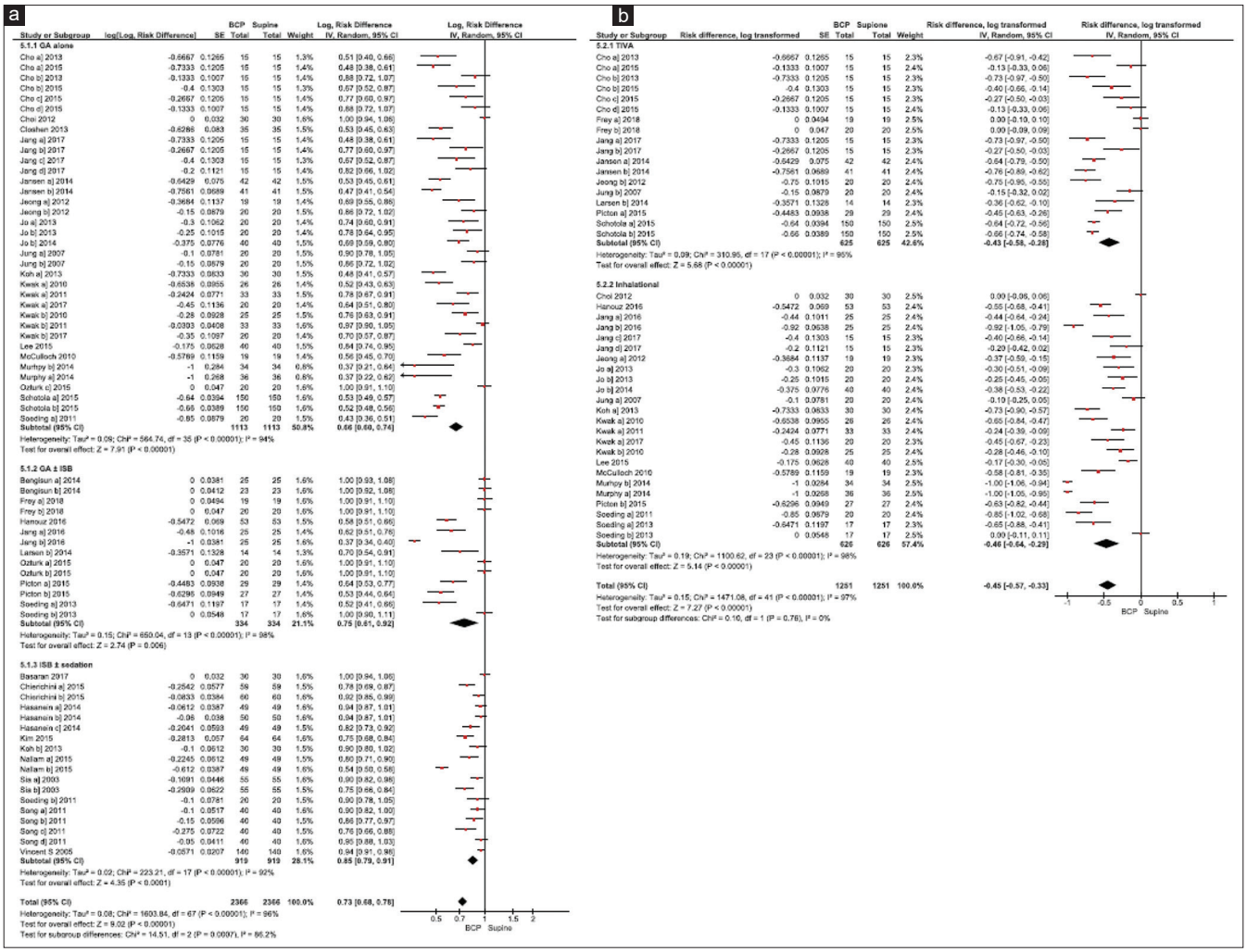
BCP - Beach chair position; BP - Blood pressure; CDE - Cerebral desaturation event; CI - Confidence intervals; DHR - Delayed heart rate; EHR - Early heart rate; GA - General anaesthesia; HBE - Hypotension bradycardia episode; HR - Heart rate; ISB - Interscalene block; MBP - Mean blood pressure; MHR - Mid heart rate; PVI - Prophylactic vasopressor infusion; rSO2 - regional cerebral oxygen saturation; SG - Study group; TIVA - Total intravenous anaesthesia.



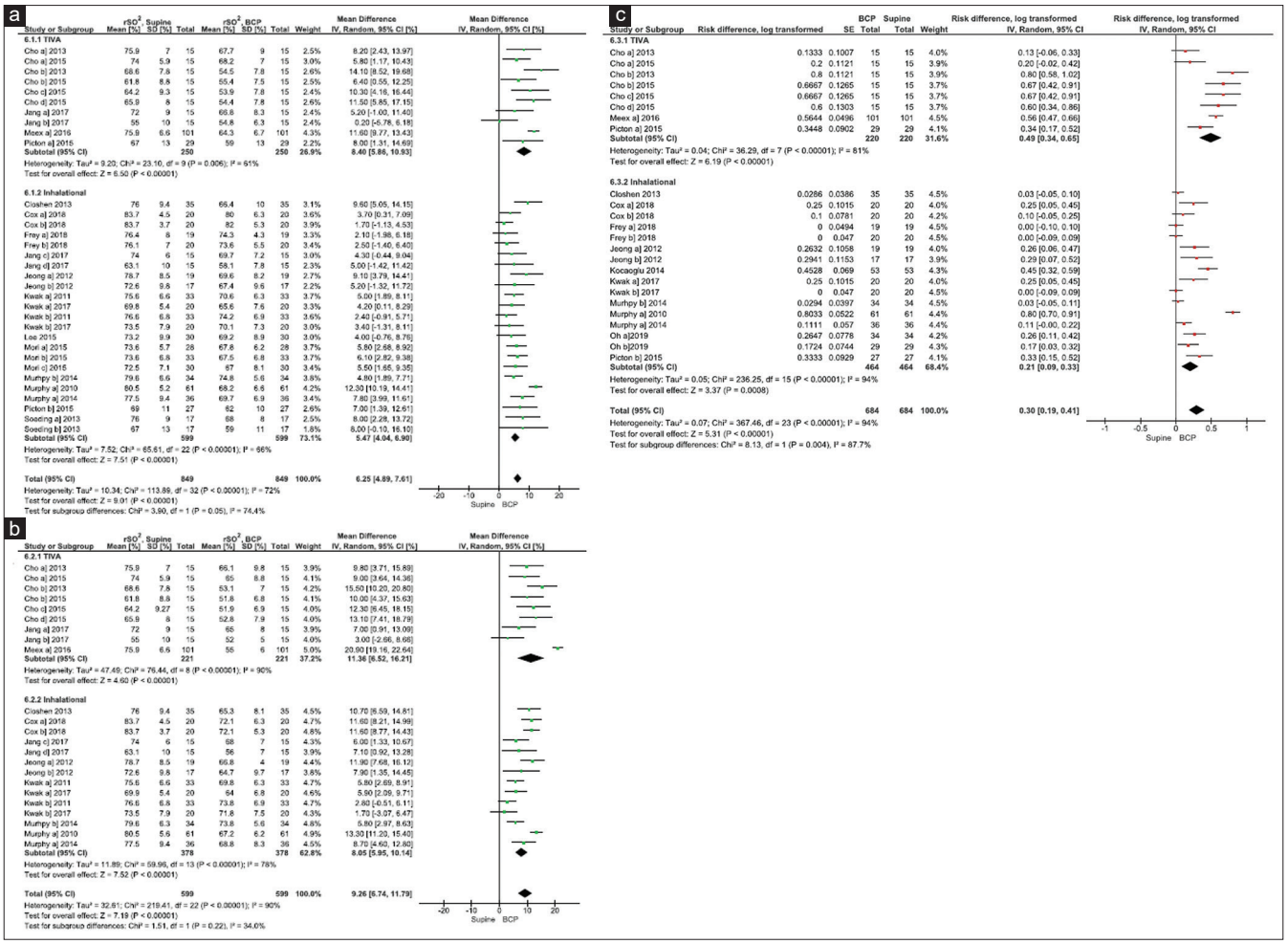
Supplementary Digital Content File 4: Risk of bias summary (a) and graph (b)

No.	Parameter	Inclusion of Meex et al,[59]	Excluding Meex et al,[59]
1	**HR fall (beats/min)**		
	Type of anaesthesia, MD (95% CI)	4.5 (2.9, 6.2)	4.2 (2.9, 5.4)
	Test for heterogeneity	$I^2 = 69\%$, $P < 0.00001$	$I^2 = 40\%$, $P < 0.004$
	Test for subgroup differences	$P = 0.28$	$P = 0.33$
2	**HR fall (beats/min)**		
	Maintenance agent, MD (95% CI)	4.9 (3.06, 6.73)	4.5(3.6, 5.9)
	Test for heterogeneity	$I^2 = 70\%$, $P < 0.00001$	$I^2 = 43\%$, $P < 0.002$
	Test for subgroup differences	$P = 0.15$	$P < 0.0001$
3	**CDEs (Incidences, log-number of subjects)**		
	Maintenance agent, MD (95% CI)	0.31 (0.19, 0.42)	0.29 (0.17, 0.41)
	Test for heterogeneity	$I^2 = 94\%$, $P < 0.00001$	$I^2 = 94\%$, $P < 0.00001$
	Test for subgroup differences	$P = 0.006$	$P = 0.02$
4	**rSO_2 (absolute fall, %)**		
	Maintenance agent, MD (95% CI)	6.3 (4.9, 7.6)	6 (4.6, 7.3)
	Test for heterogeneity	$I^2 = 72\%$, $P < 0.00001$	$I^2 = 63\%$, $P < 0.00001$
	Test for subgroup differences	$P = 0.052$	$P = 0.13$
5	**rSO_2 (lowest achieved, %)**		
	Maintenance agent, MD (95% CI)	9.3 (6.7, 11.8)	8.7 (7, 10.3)
	Test for heterogeneity	$I^2 = 90\%$, $P < 0.00001$	$I^2 = 72\%$, $P < 0.00001$
	Test for subgroup differences	$P = 0.22$	$P = 0.26$

Supplementary Digital Content File 5: Publication Bias. All the measures are MDs from pre- to post-BCP status. HR was considered for mid periods (11-30 mins of BCP) only as data for rest of the periods (EHR and DHR) did not reveal publication bias during funnel plot asymmetry evaluation and Egger's test. We observe after inclusion of study by Meex *et al*.,[59] there are no gross change in the results for most of the parameters indicating addition of this study had not influenced the data outputs. CDE - Cerebral desaturation event; CI – Confidence interval; HR - Heart rate; MD – Mean difference; rSO_2 - Regional cerebral oxygen saturation



Supplementary Digital Content 6: The figure that illustrates the forest plot depicting number of subjects experiencing the hypotension episodes with respect to (a) Type of anaesthesia (GA, GA + ISB or ISB ± sedation) (b) Maintenance agent (TIVA-propofol or inhaled anaesthesia). Meta-analysis of this parameter for pre- and post-BCP status revealed higher RD for SGs with GA than GA + ISB subjects and ISB ± sedation (test for sub-group differences $P = 0.0007$, $I^2 = 86.2\%$). However, higher observed risk was not found for subjects of TIVA-propofol over inhaled anaesthetics for developing hypotensive responses ($P = 0.76$, $I^2 = 0\%$). BCP - Beach chair position; CI - Confidence interval; GA - General anaesthesia; ISB -Interscalene block; IV - Inverse variance; RD - Risk difference; SE - Standard error; SG - Study group; TIVA - Total intravenous anaesthesia



Supplementary Digital Content File 7: The figure that illustrates the number of subjects who experienced regional CDEs. (a) Meta-analysis of pooled estimates showed statistically significant fall in absolute values of rSO_2 with both TIVA-propofol and inhalational maintenance anaesthetics (I^2 = 72%, P < 0.00001). In 4 SGs which had separate left and right cerebral hemisphere recordings, the readings of the side with maximum MDs were considered. There were no differences between sub-groups with respect to the type of maintenance agent used (I^2 = 74.4%, P = 0.05). Type of anaesthesia (GA or GA + ISB) was not considered for sub-group evaluation due to paucity of relevant publications. There was no evidence of publication bias (Egger's test, P = 0.466). (b) Lowest recorded values of CDEs were extracted from 23 SGs. Lowest MD values of CDEs, showed no sub-group differences between different maintenance agents (I^2 = 34%, P = 0.22) over 5 to 90 minutes or till the end of surgery, whichever was earlier. There was evidence of publication bias (Egger's test, P = 0.003) however without affecting overall results (refer 'publication bias', Supplementary Digital Content File 5). (c) Number of subjects who experienced CDEs were reported in 24 SGs. Sub-group analysis of number of subjects who experienced CDEs revealed that TIVA-propofol had higher RD (P = 0.004, I^2 = 87.7%). There was no evidence of publication bias (Egger's test, P = 0.257). BCP - Beach chair position; CDE – Cerebral desaturation event; CI - Confidence interval; IV - Inverse variance; ISB – Interscalene block; rSO_2- Regional cerebral oxygen saturation. SE - Standard error; TIVA - Total intravenous anaesthesia