HEMOSTATIC EFFECT OF NASAL SALINE IRRIGATION DURING ENDOSCOPIC SINUS SURGERY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Abbreviations

Notation	Description
ESS	Endoscopic sinus surgery
CRS	Chronic rhino-sinusitis
WSI / HSI	Warm saline irrigation / hot saline irrigation
RTSI / NSI	Room temperature saline irrigation / Normal saline irrigation
BS	Bleeding score
MAP	Mean arterial pressure
DS	Duration of surgery
BL	Blood loss
SS	Surgeon satisfaction score
MD	Mean difference
SMD	Standard mean difference
CI	Confidence interval
RR	Risk ratio
P	P-value
℃	Celsius
PRISMA	Preferred reporting items for systematic reviews and meta-analysis
ASA	American society of anaesthesiologist
RCT	Randomized controlled trial
FESS	Functional endoscopic sinus surgery

ABSTRAK

***Pendahuluan*:** Pembedahan Sinus Endoskopi (ESS) adalah cara rawatan utama bagi penyakit Rhino-sinusitis Kronik (CRS). Visual anatomi yang jelas semasa pembedahan Sinus Endoskopi (ESS) memainkan peranan penting bagi memastikan kejayaan pembedahan tanpa sebarang komplikasi. Hal ini sedemikian kerana visual anatomi yang jelas dan pengawalan pendarahan pesakit membantu pakar bedah mengenalpasti struktur anatomi dengan tepat dan menjayakan sesuatu pembedahan. Pada masa yang sama, 'Nasal Saline Irrigation' adalah satu teknik lain yang telah dikenal pasti dapat mengurangkan pendarahan pesakit semasa pembedahan Sinus Endoskopi (ESS).

***Objektif*:** Tujuan penyelidikan ini adalah untuk mengenalpasti suhu terbaik dan optimum untuk 'Nasal Saline Irrigation' semasa pembedahan Sinus Endoskopi (ESS) dijalankan bagi mengurangkan komplikasi yang sedia maklum. Selain itu, penyelidikan ini juga akan meneliti keberkesanan faktor-faktor lain untuk kawalan pendarahan dan untuk meningkatkan kualiti pembedahan 'Sinus Endoskopi' (ESS).

***Kaedah*:** Tiga penyelidik telah memilih artikel-artikel yang khusus dan tepat untuk kajian sistematik dari empat pangkalan data bebas iaitu PubMed, SCOPUS, Google Scholar dan Cochrane dari bulan Mac hingga September 2018. Setelah tamat pemilihan artikel-artikel tersebut, penyelidik telah membuat tapisan selanjutnya mengikut kriteria yang telah ditetapkan. Penyelidikan ini telah membahagikan pesakit terlibat kepada dua kumpulan iaitu 'Warm saline irrigation/ Hot Saline Irrigation' (WSI/HSI) dan 'Room Temperature Saline Irrigation/Normal Saline Irrigation' (RTSI/NSI). Faktor-faktor utama telah dibahagi kepada faktor primer dan sekunder untuk proses meta-analisis seterusnya. Antara faktor utama yang dibandingkan adalah skor pembedahan, min

tekanan arteri, jangka masa pembedahan, jumlah kehilangan darah pesakit dan skor kepuasan oleh pakar bedah.

***Keputusan*:** Tiga kajian yang melibatkan 212 pesakit telah dipilih bagi kajian sistematik. Penyelidikan ini menunjukkan bahawa secara umumnya WSI/HSI mengurangkan komplikasi pembedahan berbanding dengan RTSI/NSI. Secara amnya, nilai P yang telah didapati dari kajian ini (P <.001) menyokong kenyataan di atas. Penyelidikan ini menunjukkan bahawa kadar kehilangan darah semasa pembedahan berpandukan jadual Boezaart lebih menyokong kumpulan WSI/HSI (MD= -0.51, 95% CI [-0.84,-0.18], P<.003, I^2=72%). Seterusnya, penyelidikan ini mendapati bahawa tiada perbezaan yang ketara antara kedua-dua kumpulan di atas semasa perbandingan berkenaan dengan bacaan tekanan darah arteri pesakit (MD= -0.60, 95% CI [-2.17, 0.97], P=0.45, I^2=0%). Manakala, skor yang diberi oleh Pakar Bedah menunjukkan terdapat penurunan yang ketara dalam pendarahan WSI / HSI berbanding dengan RTSI / NSI dalam kajian (0.18, 95% CI [0.09, 0.33] P<0.001, $I^{2=}$ 0%). Selain itu, penyelidikan ini mendapati bahawa jumlah kehilangan darah pesakit adalah jauh lebih tinggi dalam kumpulan di bawah RTSI / NSI berbanding HSI / WSI (MD-56.4, 95% CI[-57.30, -55.51], P<0.001,I^2=0%). Akhir sekali, penyelidikan ini mendapati faktor tempoh pembedahan menunjukkan peningkatan yang ketara dalam kumpulan RTSI / NSI daripada kumpulan HSI / WSI dalam semua kajian yang telah dibuat (MD= -9.02, 95% CI [-11.76, -6,28], P<0.001, I^2=0%).

***Kesimpulan*:** Kajian sistematik dan meta-analisis ini ternyata membuktikan bahawa pesakit kumpulan WSI / HSI memperoleh manfaat yang lebih semasa pembedahan ESS berbanding dengan pesakit kumpulan RTSI / NSI. Akhir sekali, hanya sebilangan kecil pesakit telah dikaji sepanjang penyelidikan ini. Oleh itu, penyelidikan

yang melibatkan kumpulan pesakit yang ramai akan diperlukan untuk mendapatkan analisis yang lebih tepat.

Kata Kunci**:** *hemostasis, nasal saline, irrigation, endoscopic sinus surgery, chronic rhinosinusitis, intraoperative bleeding.*

Tahap Bukti**:** *1A*

ABSTRACT

Introduction: Intraoperative hemostasis is crucial for adequate anatomical visualization during endoscopic sinus surgery (ESS) and has been identified as gold-standard treatment for medically refractory chronic rhinosinusitis (CRS). Effective surgery is termed upon adequate identification of anatomic structures, good surgical visualization and controlled bleeding throughout the surgery. Nasal saline irrigation is a novel technique to reduced intra-operative bleeding during endoscopic sinus surgery.

Objective: The aim of this research is to assess the suitable and optimum temperature for nasal saline irrigation during endoscopic sinus surgery with regards to bleeding control and quality of surgery site during endoscopic sinus surgery(ESS).

Methods: Three authors independently conducted an electronic search via (PubMed, SCOPUS, Google Scholar) and (Cochrane) from their origination to September 2018. The included studies compared nasal saline irrigation (hot saline /warm saline irrigation (HSI/WSI) versus room temperature/normal saline irrigation (RTSI/NSI) during ESS. The outcomes of interest were bleeding score(BS), mean arterial pressure(MAP), duration of the surgery(DS), blood loss (BL), and the surgeon satisfaction score (SS).

Results: Based on three studies with a total of 212 patients providing the data, we found that WSI/ HSI produced a better outcome compared to the RTSI/NSI group in the surgical field quality (Mean Difference (MD)= -0.51, 95% CI [-0.84,-0.18], P<.003, I^2=72%), 3 studies consisting 237 patients ;moderate certainty. There was no significant difference between the two comparison group in regard to mean arterial pressure (Mean Difference(MD)= -0.60, 95% CI [-2.17, 0.97], P=0.45, I^2=0% , 3 studies with 237 patients; moderate certainty. The surgeons' satisfaction about the significant reduction in bleeding during the operation showed that there was significant

decrease in bleeding in WSI/HSI compared to RTSI/NSI in two studies (Risk ratio = 0.18, 95% CI [0.09, 0.33] P<0.001, $I^{2=}$ 0% , 2 studies with 175 patients ; moderate certainty). The volume of blood loss was also significantly higher in groups under RTSI/NSI than HSI/WSI in all the studies reviewed **(**Mean Difference (MD)=56.4, 95% CI[-57.30, -55.51], P<0.001,I^2=0%; moderate certainty). The duration of surgery showed significant increase in RTSI/NSI group than HSI/WSI group in all the studies (Mean Difference (MD)= -9.02, 95% CI [-11.76, -6,28], P<0.001, I^2=0% , 3 studies with 237 patients ; moderate certainty).

Conclusion: The evidence from this review suggests that WSI/HSI group are statistically better compared to RTSI/NSI group. Also, no beneficial or detrimental effect of surgeons' satisfaction score could be determined based on existing evidence. However, since very small number of studies were recruited, further trials are needed to establish the results of this study.

Keyword*: hemostasis, nasal saline, irrigation, endoscopic sinus surgery, chronic rhinosinusitis.*

Level of evidence*: 1A*

1.0 INTRODUCTION

Rhinosinusitis is an inflammatory condition of the mucosa of the nose and paranasal sinuses of multifactorial etiology. It is termed chronic rhinosinusitis (CRS) when the condition persists for at least 12 weeks without complete resolution. It is diagnosed in patients with a distinct set of symptoms and signs as defined by European Position Paper on Rhinosinusitis and Nasal Polyps 2020 (EPOS) guidelines[1]. It is further divided into two major phenotypes: CRS with or without polyps (CRSwNP or CRSsNP, respectively).

The goal of CRS management is to restore the functional integrity of the inflamed mucosal lining and improve the patient's quality of life[2]. The management of CRSsNP and CRSwNP are distinct in the current EPOS guidelines, referred according to the differences in their underlying etiology and pathophysiology. Medical therapy is the primary treatment modality for both pathways. In general, in mild disease, topical steroids and saline irrigation form the mainstay treatment. In more severe cases, under specialist care, low dose antibiotics may be considered, and in CRSwNP systemic steroids also play an important role. If maximal medical treatment fails, a CT scan of the sinuses is performed to confirm the correct diagnosis and surgical intervention may be considered. Endoscopic sinus surgery (ESS) is recommended when optimal medical treatment has failed; persistent symptoms despite either a three month trial of nasal irrigation, topical steroids with or without long-term antibiotics in CRSsNP, or a 3-month course of nasal steroid spray or drops in mild or moderate CRSwNP, or 1 month of medical treatment including systemic and topical steroids with doxycycline in severe CRSwNP. ESS has been identified to be the standard procedure for nasal obstruction, with moderate improvement in facial pain and post-nasal drip[3]. Meanwhile, hyposmia and headache were said to improve the least [4]. Endoscopic sinus surgery is the gold

standard and minimally invasive established procedure to treat medically refractory CRS patients[5-9].

ESS, pioneered by Stammberger and Kennedy in 1985, describes a minimally invasive mucosal sparing endoscopic approach to the sinuses; preserving mucosa while enlarging natural drainage pathways and removing bony partitions in the ethmoid sinuses, with the aim of improving sinus ventilation, mucociliary function and improving topical access to sinus mucosa. Also, RCT evidence is limited, as randomization and blinding are difficult during various types ESS.

Intraoperative hemostasis in endoscopic sinus surgery is anticipated to be a moderate risk bleeding surgery. Bleeding is expected to become the largest obstacle to endoscopic visualization and thus it leads to inadvertent complications namely brain injury, orbital or optic nerve injury, and severe bleeding from major vessel in the nasal region[10-14].

There are several techniques used by sinus surgeons in order to reduce intraoperative hemostasis[15-17]. However, the ideal technique has yet to be comprehensively described in a single publication and there are conflicting evidence in the literature on which method works the best.

Saline irrigation is best known for the management of posterior epistaxis[18]. The hemostatic mechanism of saline irrigation is not obvious and may be due to: edema and narrowing of the intranasal lumen with pressure being exerted on the injured vessel; reducing the blood outflow and the intraluminal blood pressure caused by mucosal vasodilatation and cleaning of nasal blood clot. Saline irrigation for epistaxis was found to be easy, less painful and less traumatic to the nose than nasal packing[19]. Therefore, this method was introduced to reduce the intraoperative bleeding. Besides, saline irrigation ranging from 40-50 ℃ has shown to decrease diffuse oozing from sinonasal

mucosa and intracranial bleeding from small vessels. Another advantage of the proposed saline irrigation is that it helps with the cleaning of the endoscopic lens[19] Saline irrigation fluid is also believed to increase the clotting cascade mechanism in the human body and this in turn reduces bleeding during surgery[20]

The aim of this meta-analysis and systematic review is to better understand the suitability and optimum temperature of the nasal saline irrigation during ESS can affect intraoperative blood loss, thereby leading to an improved surgical field, diminished complications profile, decreased requirements of multiple surgeries and better outcomes for the patients. Surgeons' satisfaction score, hemodynamic instability such mean arterial pressure, overall duration of the surgery, blood loss of the patient were also compared as a secondary outcomes .

2.0 METHODOLOGY

Registered protocol

The review protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) database under registration number **CRD42019117083**. The method and reporting were based on Cochrane collaboration [21] and the preferred reporting items for systematic reviews and meta analysis statement[22]. The evaluation was done according to the Grading of Recommendation Assessment, Development and Evaluation (GRADE) guideline[23].

2.1 Eligibility criteria

Randomized controlled trials (RCTs) comparing WSI/HSI with RTSI/NSI, placebo, and other standard treatment (tranexamic acid) were included. Cross over studies were excluded due to the carry over effect. Randomized controlled trials that met the following inclusion criteria were eligible:

1. Studies with adults (19 years of age and over) diagnosed with chronic rhinosinusitis with or without nasal polyposis of either gender or ethnicity .

2. The trials studied adult chronic rhinosinusitis patients receiving endoscic sinus surgery with the intraoperative nasal saline irrigation varying in absolute warm/ hot saline irrigation in comparison with room temperature / normal saline irrigation.

3. Studies in which comparison made with other hemostatic agent such as cocaine or adrenaline were excluded.

4. Both primary and secondary outcomes were compared intra-operatively.

2.2 Search strategy

A search for the literature intended for this review was performed using ; **CENTRAL** (Cochrane Central Register of Controlled Trials), **SCOPUS**, **PUBMED**, and **GOOGLE SCHOLAR** . Importantly, only articles that fulfilled the conditions discussed in the the following sections were included:

Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement was used as guide to identify all available studies related to variant of intra operative nasal irrigation written in English from the inception up to September of 2018. Three authors independently conducted the literature search using the search terms “hemorrhage”, “hemostasis”, “nasal saline” ,” irrigation”, “endoscopic sinus surgery” “chronic rhinosinusitis”, “intraoperative blood loss” and “ hemorrhage”. The systematic search for relevant original articles was based on the topic area used in the search in alternating combinations and linked via the operators “AND” and “OR”. We complemented the keyword-based searches by using also the available MeSH (Medical Subject Headings) dictionary. No restrictions were made in terms of period of publication and study duration. Furthermore, only the studies published in English and those having human subjects of investigation were incorporated in the search. We checked the reference list of identified RCTs and review articles to find unpublished trials or trials not identified by electronic searches. We searched for ongoing trials through the World Health Organization International Clinical Registry Platform; *www.clinicaltrial.gov*

2.3 Study selection

Review authors (DN, KYC) screened the titles and abstracts from the searches and obtained full text articles when they appeared to meet the eligibility criteria or when there was missing or incomplete data to assess the eligibility. Attempts were made to retrieve further details directly from the authors when needed. Studies were excluded from the analysis if the outcome of involvement was not clearly stated with quantifiable data or if it was not possible to extract and calculate the appropriate data from the published results. All the reasons for the exclusion were documented appropriately. Any disagreement between review authors were resolved by third author (BA).

2.4 Data extraction

Data from eligible studies were extracted using standardized forms and were independently checked by three reviewers(DN,BA,NH). The reviewers independently extracted the trial characteristics (single or multi centre study type), baseline characteristics of the patients (age, gender, American Society of Anesthesiologist [ASA], types of surgery), inclusion and exclusion criteria, the description of the intervention (types of anaesthesia, mean arterial pressure and irrigation administration) and outcomes. The primary outcomes were based on bleeding scores by the Boezaart endoscopic score (BS). The secondary outcomes were mean arterial pressure (MAP), duration of the surgery (DS), blood loss (BL), surgeon satisfaction score (SC) regarding significant decrease in bleeding. These outcomes were compared between the treatment group, which received warm saline/ hot saline nasal irrigation (47- 50℃) and the control group which received room temperature/ normal saline irrigation (18-20℃). From the studies marked for inclusion, we extracted data regarding patient number, grading scale used, nasal saline irrigation variables and the ***P*** value recorded for the comparison

between the treatment group and the control group. The risk of bias for each study was analysed using the Cochrane risk of bias tool.

2.5 Risk of bias assessment

Two review authors (DN and KYC) independently assessed risk of bias of the included study using the risk of bias assessment tool in the Cochrane Handbook for systematic Reviews of Interventions (Higgins 2011). We resolved any disagreement by discussion and consultation with the third person(BA) and sometimes a fourth person (NH). The following items were independently assessed by two authors (DN and KYC) using the risk of bias assessment tool (Higgins 2011) (Appendix 2).

- Was there adequate sequence generation(selection bias)?
- Was allocation adequately concealed(selection bias)?
- Was knowledge of the allocated interventions adequately prevented during the study?
  - Participants and personnel (performance bias)
  - Outcome assessors (detection bias)
- Were incomplete outcome data adequately addressed (attrition bias)?
- Are reports of the study free of suggestion of selective outcome reporting (reporting bias)?
- Was the study apparently free of other problems that could put it at a risk of bias ?

We used the Cochrane 'Risk of bias' tool in RevMan 2014, which involves describing each of these domains as reported in the study and then assigning a judgement about the adequacy of each entry: 'low', 'high' or 'unclear' risk of bias. Lack of blinding in itself will be sufficient to label a study as at high risk of bias if all outcomes are subjective, e.g. surgeon reporting of clarity of field

2.6 Grading quality of evidence

Two authors (DN and KYC) independently applied the GRADE approach to rate the overall quality of evidence. The quality of evidence reflects the extent to which we are confident that an estimate of effect is correct and we will apply this in the interpretation of results[24].

There are four possible ratings: high, moderate, low and very low. A rating of high quality of evidence implies that we are confident in our estimate of effect and that further research is very unlikely to change our confidence in the estimate of effect. A rating of very low quality implies that any estimate of effect obtained is very uncertain.

The GRADE approach rates evidence from RCTs that do not have serious limitations as high quality. However, several factors can lead to the downgrading of the evidence to moderate, low or very low[25]. The degree of downgrading is determined by the seriousness of these factors:

- Study limitations (risk of bias);
- Inconsistency;
- Indirectness of evidence
- Imprecision
- Publication bias.

2.7 Statistical analysis

i. Measures of treatment effect

For continuous outcomes we reported the mean difference (MD) with standard deviation (SD) or, when necessary, the standardised mean difference (SMD). We anticipated that different intraoperative bleeding scales would have been used in different studies: namely the Boezaart scale. We used the standardised mean difference as the summary statistic to standardise the results of studies to a uniform scale.

In the case of dichotomous outcomes, we calculated the risk ratio (RR) and odds ratio (OR) with 95% confidence interval (CI).

ii. Unit of analysis issues

We determined appropriate units of analysis from the included studies.

iii. Cluster-randomised trials

We analysed cluster-randomised trials based on the level of allocation, i.e. clusters of participants.

iv. Multi-armed trials

When analysing multi-armed trials, we combined all relevant experimental intervention groups in the study into a single group and all relevant control intervention groups into a single control group. If we consider one of the arms to be irrelevant, we excluded it from analysis (e.g., tranexamic acid arm).

For dichotomous outcomes, we calculated both the sample sizes and the numbers of people with events across groups. For continuous outcomes, we combined means and standard deviations using the methods described in Chapter 7 (section 7.7.3.8) of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

v. Dealing with missing data

We contacted the study authors via email whenever the outcome of interest is not reported if the methods of the study suggest that the outcome was measured. We did the same if not all data required for meta-analysis are reported, unless the missing data are standard deviations. If standard deviation data are not available we would approximate these using standard estimation methods: from P values, standard errors or 95% CIs if these are reported, as detailed in the *Cochrane Handbook for Systematic Reviews of Interventions* (Handbook 2011). Where it is impossible to estimate these, we contacted the study authors.

Apart from imputations for missing standard deviations, we did not conduct any other imputations. We extracted and analysed data for all outcomes using the available case analysis method.

vi. Assessment of heterogeneity

We assessed the clinical heterogeneity (which may be present even in the absence of statistical heterogeneity) by examining the included trials for potential differences between studies in the types of participants recruited (including type of operation), interventions or controls used and the outcomes measured.

We assessed statistical heterogeneity by visually inspecting the forest plots and by considering the Chi^2 test (with a significance level set at $P < 0.10$) and the I^2 statistic, which calculates the percentage of variability that is due to heterogeneity rather than chance, with I^2 values over 50% suggesting substantial heterogeneity (Handbook 2011).

vii. Assessment of reporting biases

We did not create a funnel plot to detect reporting biases as only 3 studies were included in the meta-analysis. We assessed reporting bias as between-study publication bias and within-study outcome reporting bias. If we identify small studies with larger treatment effects, we would perform a sensitivity analysis excluding these studies.

viii. Data synthesis

We used the Cochrane software package RevMan 5 for quantitative meta-analysis of the extracted data (RevMan 2014). We expressed continuous data as the MD or SMD with 95% CI. We revealed dichotomous data as the RR or OR with 95% CI. We pooled the results using a random-effects model because we expect there to be substantial clinical heterogeneity.

ix. Subgroup analysis and investigation of heterogeneity

Where data are available, we plan to conduct some subgroup analyses regardless of whether statistical heterogeneity is observed, as these are widely suspected to be potential effect modifiers. For this review, this includes the following:

- Different volume of nasal saline irrigation administration (20 mL versus 50 mL);
- Patients with chronic rhinosinusitis with and without nasal polyps;
- Patients that use local corticosteroids in the month before surgery versus no corticosteroids;
- Different forms of anaesthesia and other intraoperative interventions;
- Patients with thromboembolic prophylaxis versus patients without thromboembolic prophylaxis;

x. Sensitivity analysis

We intended to carry out sensitivity analyses on the basis of the methodological diversity of the included studies. We considered the following when repeating the analysis:

- Excluding studies with high risk of bias (defined as four out of seven domains deemed to have high risk)
- Excluding small studies with larger treatment effects;

2.8 Ethical approval

This thesis did not involve any ethical requirements. Since this is a systematic review and meta-analysis, an ethical requirement is not mandatory.

3.0 Results and Analysis

3.1 Study Selection

A total of 256 references were identified from the searches: 3 of these were removed because of duplicate and clearly irrelevant references, 250 of the remainder were excluded due to title and abstract, leaving 3 full-texts for further consideration. A flow chart of study retrieval and selection is provided in Figure 1.

The final analysis included 237 patients (3 articles) published between 2014 and 2016.Three studies were identified; Shehata et al [26], Al-Ississ et al[27]and Gan et al[28]. All these studies compared the effects of different temperature of nasal saline irrigation in order to improve the quality of surgical field. All the studies recruited adult participants. Some studies used intra-patient controls: each patient had both nasal cavities that received same interventions; every patient provided two samples[27]. In other studies, each patient was regarded as one sample, as each patient received only one kind of intervention. One of the study included tranexamic acid as another comparison[26]. The characteristics of all included studies in the analysis are summarized in Table 1.

Figure 1: Flow diagram of study selection

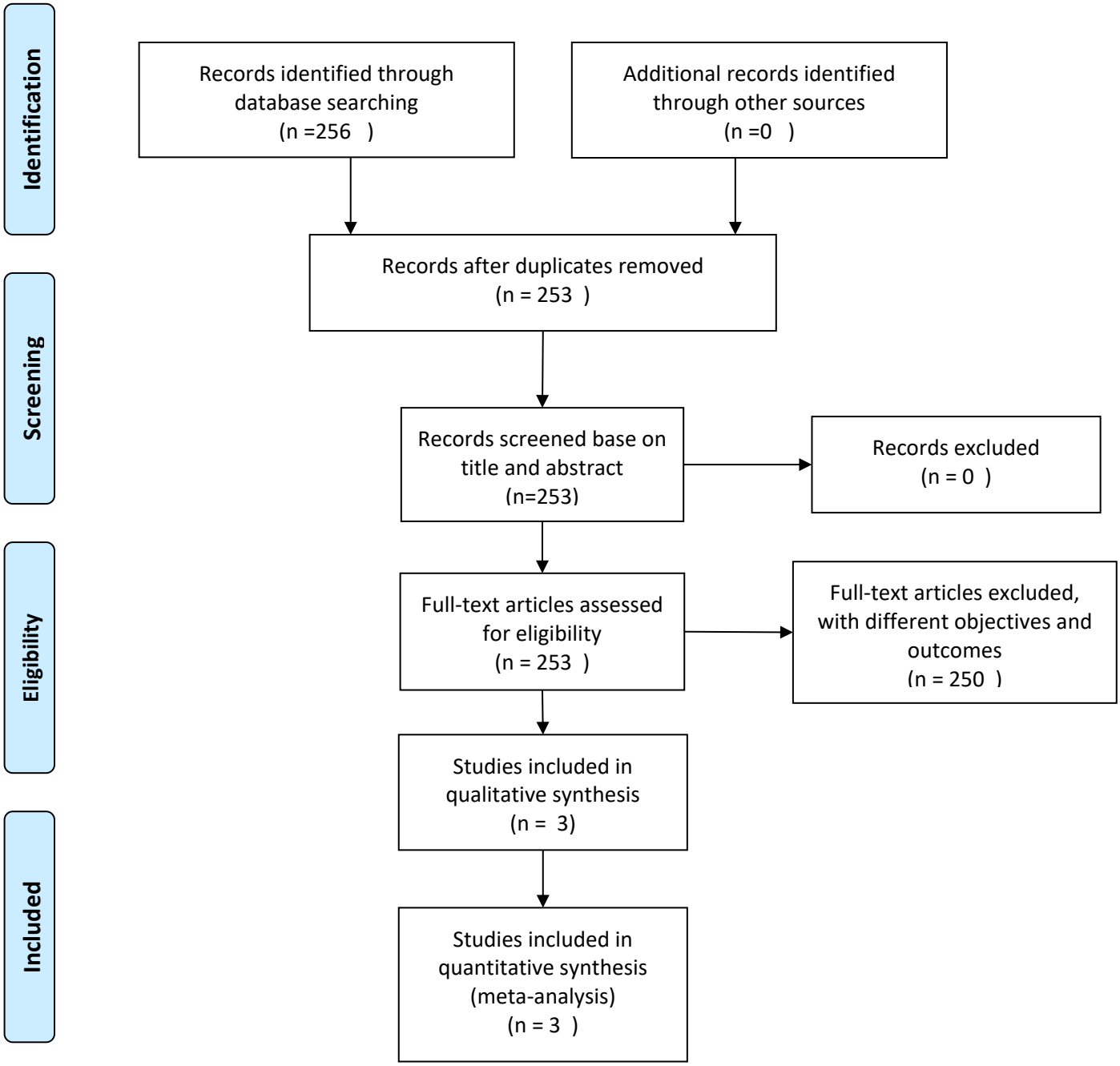

Table 3.1 : Characteristics of included studies

Author	Published year	Study type	Age range/ mean (years)	Total patients	Surgical procedure	Intervention	Outcomes		Other Results
							Group 1 (warm/hot saline) (WSI/HSI)	**Group 2 (room temperature)(RTSI)/ Normal saline (NSI)**	
***Shehata*[26]**	2014	RCT	20- 50 years	75	FESS	HSI (50 DC) Group B Vs NSI (20 DC) Group C	*Significant decrease in BS,BL, DS,	* Significant increase in BS,BL,DS	1.MAP- no difference 2.Coagulation profile- no difference 3.Surgeon's score- significant reduction of bleeding in HS, 4.Nausea 4%
***Al-Ississ*[27]**	2016	RCT	28-58 years	100	FESS Septo-rhinoplasty	WSI (48 DC) Vs NSI (20 DC)	*Significant decrease in BS,BL, DS	* Significant increase in BS,BL,DS	1. MAP no difference 2. Surgeon's score-reduction of bleeding in WS - BS I& II > frequent in

									Group 1 -Score 3 & 4 > in Group 2 -BS 5 was both 0% in both groups
Gan[28]	2014	RCT (double blinded)	19 years and above	62	FESS	WSI (49 DC) Vs RTSI(18 DC)	BS -No difference DS- No difference BL- lower than group 2	BL- higher	1. Heart rate- no difference 2. MAP- no difference 3. Operating time- no difference 4. Short cases >120mins- no difference in BS 5. Long cases >120mins- group 2 has higher BS

Randomized controlled trials(RCT), Functional endoscopic sinus surgery(FESS), hot saline irrigation (HSI),warm saline irrigation (WSI), room temperature saline irrigation(RTSI), Boezaart score (BS), duration of surgery(DS), blood loss(BL) , mean arterial pressure(MAP)

3.2 Participants

A total of 237 chronic rhinosinusitis patients who failed maximal medical treatment and underwent endoscopic sinus surgery were the target focus of the study. The characteristics of the those included studies are shown in Table 1. All the studies were single centre-studies which covered different continents (Asian and American) namely cities of Benha (Egypt), Amman (Jordan) and Vancouver (Canada). Two studies reported the mean age for the treatment and control groups were 20 to 58 years [26-27]. Meanwhile, another study reported the overall mean age group was at least 19 and above[28]. Both male and female participants were included in this study[26-28]. All the 237 patients were categorized as class I and II by the American Society Of Anaesthesiologist (ASA) and scheduled for either functional endoscopic sinus surgery[26-28] or septorhinoplasty[27]. One study had 3 treatment arms[a] while both the other studies had two treatment arms[27-28].

3.3 Interventions

Participants in the studies were randomized in either two[27-28] or three groups[26]. There were 3 studies with two treatment groups. The first study evaluvated hot saline irrigation (50 ℃) and normal saline irrigation (20℃)[26-28]. The second study compared warm saline (48 ℃) with normal saline irrigation (20℃)[27]. Finally, the last study compared warm saline (49℃) with room temperature saline irrigation (18℃)[28].

All the studies specified that their patients were induced under general anaesthesia with intravenous propofol. The patients' mean arterial pressure was kept in between 50 - 75 mmHg during the procedure.

There were a few extra procedures which were observed in these 3 studies. For example, in a study included, muscle relaxant was reversed with atropine (0.02mg/kg) and neostigmine (0.05mg/kg) after surgery[26]. Meanwhile, another study reported the mean arterial pressure was maintained by administration of nitroglycerine infusion (5-10mcg/kg/min) with incremental boluses of 5mg labetalol[27]. This was followed by placement of endotracheal intubation, nasopharyngeal gauze pack to avoid the blood from flowing into oropharynx, nasopharynx and further into larynx. One of the study mentioned that both the nasal cavities were packed with neuro-patties soaked with Ottrivin (Xylomethazolin 0.05%) and patients were positioned in RTP, with their heads elevated 15 degrees above the horizontal axis of the operating table[28]. These different observations were deemed not to affect the result of this research.

3.4 Risk of bias in included studies

Risk of bias was done on all the studies based on the Cochrane Handbook . The risk of bias for the trials was classified into low risk, unclear risk or high risk. The seven domains of risk of bias were assessed. They are random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and other bias. One study did not report on risk of bias assessment in their study (Figure 7, Figure 8)[26].

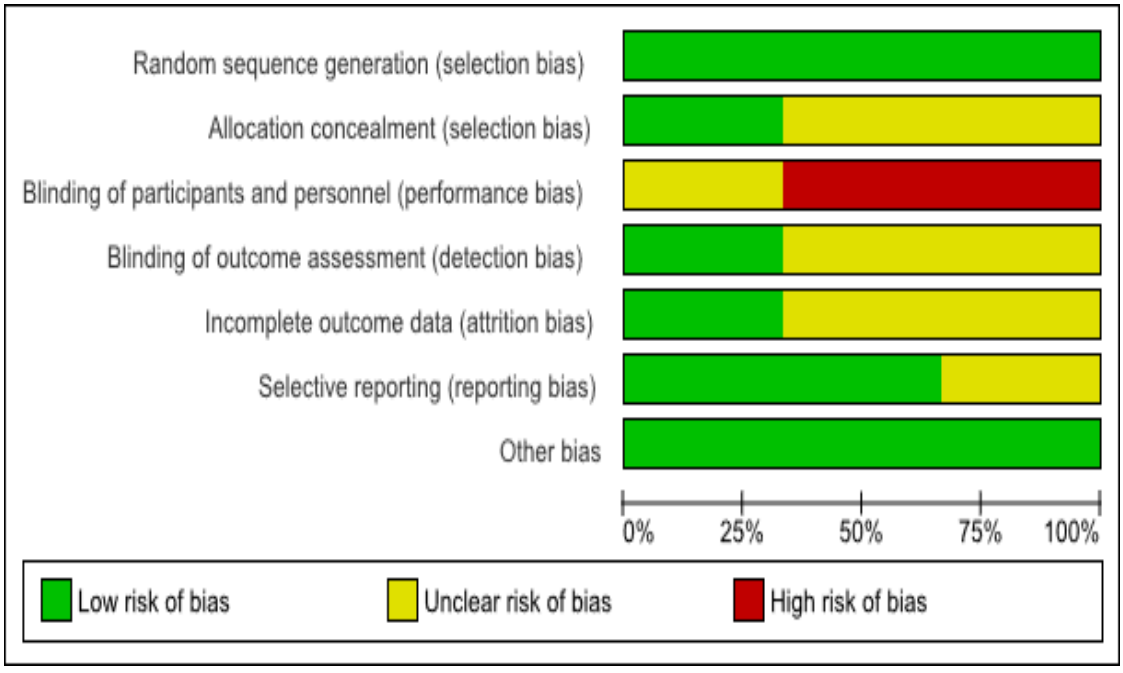

Figure 2 : Risk of Bias Graph

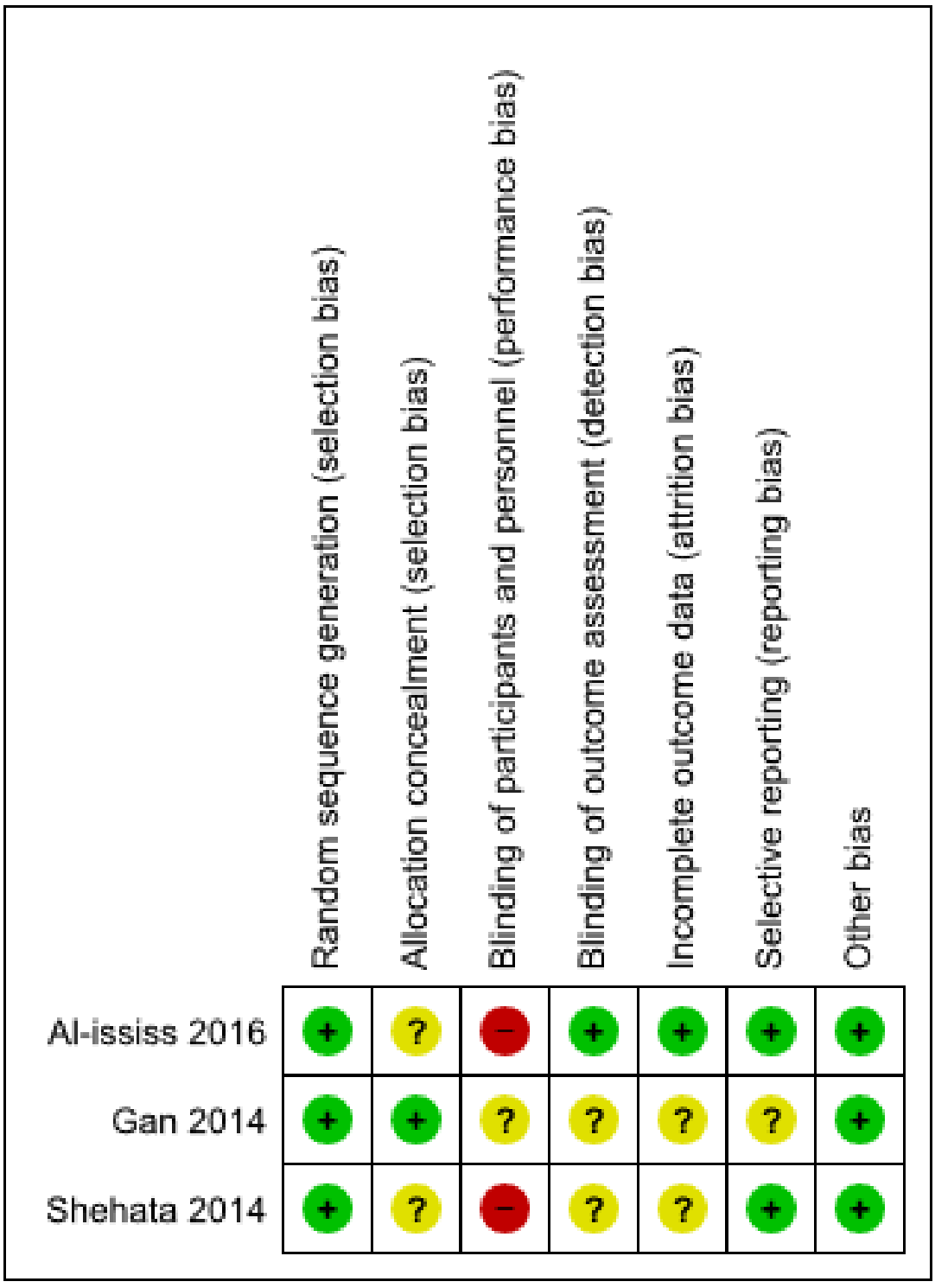

Figure 3 : Risk of Bias Summary

Random sequence sampling

All the three studies had low risk of random sequence generation.

Allocation concealment

One of our three studies had low risk of allocation concealment as compared to 2 other studies which remained unclear[27].

Blinding of participants and personnel

Two study did not report if the participants and the medical personnel were blinded or not, so this resulted in 'high risk' performance bias[27-28]. In addition, the detection was unclear in both the studies because not all outcomes were blinded.

Incomplete outcome

Although it is unclear whether some patients were excluded either pre or post intervention we considered this to be an unclear risk to selection bias[26-28].

Selective reporting bias

The protocol for all the studies were not provided. However, all three studies reported the outcomes specified in their respective methodology and hence the risk was classified as low bias. However one study did not report all the outcome thus we judged as unclear risk of bias[28].

Other bias

We did not detect any other possible sources of bias.

3.5 Outcomes

The primary and secondary outcomes were reported in all three studies [26-28] . Three studies measured primary outcomes with Boezaart bleeding score [26-28]. The tool for assessing the bleeding score was developed by Boezaart[table 2].

The surgical field was first suctioned clear of blood and then graded by the surgeon using the above validated scale. This is a scale from 0 to 5 that was used to outline the amount of suction required to clear the area of blood that obstructs the visual field. A score of 0 was given for an area with no bleeding, 1 for slight bleeding where no suction required, 2 for slight bleeding requiring suction, 3 for moderate bleeding that improves for several seconds once suction has occurred, 4 for moderate bleeding that restarts directly after suctioning and 5 for severe bleeding that occurs faster than blood can be removed.

Secondary outcomes were additional outcomes monitored to help interpret the results of the primary outcome. They are as below:

- **Hemodynamic parameters**

  MAP and heart rate were recorded every 10-15 minutes as the most important source of bleeding during endoscopic sinus surgeries is the capillaries[26-28].

- **Total blood loss in milliliters (ml)**

  [Time Frame: from the start of surgery to the end of surgery, up to 6 hours]

  Estimated blood loss in millilitres per hour is calculated by subtracting the volume of total irrigation used during the case from the total amount of fluid in the suction canister at the end of surgery and dividing by surgical time in hours[26-28].

- **Duration of surgery in minutes**

- **Surgeon's Satisfaction Rating Scale (SC)**

  [Time Frame: at the end of surgery (up to 6 hours)] . However one study did not report on surgeons satisfaction score [28]. Other parameters such as coagulation profile was measure in a study[26]. Out of these studies, one study reported on short cases(<120 mins) versus long cases (>120 mins)[27].

3.6 Comparisons and effects of intervention

There were two(HSI/WSI versus RTSI/NSI) comparisons in this review and for each comparison, the primary and secondary outcomes were assessed. The results of the research are tabulated in Summary of Findings -(Table 2).

There were 3 modes of temperature selected in this review and for each comparison, the primary and secondary outcomes were assessed.

i. Hot saline irrigation (50℃) versus normal saline irrigation (20℃)[26]
ii. Warm saline irrigation (48℃) versus normal saline irrigation(20℃)[27]
iii. Warm saline irrigation (49 ℃) versus room temperature saline irrigation (18 ℃)[28]