



## Effectiveness of heparin versus 0.9% saline solution in maintaining the permeability of central venous catheters: a systematic review\*

Eficácia da heparina e soro fisiológico para manter a permeabilidade dos cateteres venosos centrais: revisão sistemática

Efectividad de la heparina y el suero fisiológico para mantener la permeabilidad de los catéteres venosos centrales: revisión sistemática

Eduardo José Ferreira dos Santos<sup>1</sup>, Maria Madalena Jesus Cunha Nunes<sup>2</sup>, Daniela Filipa Batista Cardoso<sup>1</sup>, João Luís Alves Apóstolo<sup>1</sup>, Paulo Joaquim Pina Queirós<sup>1</sup>, Manuel Alves Rodrigues<sup>1</sup>

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<sup>1</sup> Escola Superior de Enfermagem de Coimbra, Unidade de Investigação em Ciências da Saúde, Coimbra, Portugal.

<sup>2</sup> Instituto Politécnico de Viseu, Centro de Estudos em Educação, Tecnologias e Saúde, Viseu, Portugal.

### ABSTRACT

**Objective:** Determining which is the most effective solution (heparin flush compared to 0.9% saline flush) for reducing the risk of occlusions in central venous catheters (CVC) in adults. **Method:** The systematic review followed the principles proposed by the Cochrane Handbook; critical analysis, extraction and synthesis of data were performed by two independent researchers; statistical analysis was performed using the RevMan program 5.2.8. **Results:** Eight randomized controlled trials and one cohort study were included and the results of the meta-analysis showed no difference (RR=0.68, 95% CI=0.41-1.10;  $p=0.12$ ). Analysis by subgroups showed that there was no difference in fully deployed CVC (RR=1.09, CI 95%=0.53-2.22;  $p=0.82$ ); Multi-Lumen CVC showed beneficial effects in the heparin group (RR=0.53, CI 95%=0.29-0.95;  $p=0.03$ ); in Double-Lumen CVC for hemodialysis (RR=1.18, CI 95%=0.08-17.82;  $p=0.90$ ) and Peripherally inserted CVC (RR=0.14, CI 95%=0.01-2.60;  $p=0.19$ ) also showed no difference. **Conclusion:** Saline solution is sufficient for maintaining patency of the central venous catheter, preventing the risks associated with heparin administration.

### DESCRIPTORS

Catheterization, Central Venous; Heparin; Sodium Chloride; Central Venous Catheters; Review.

### Corresponding author:

Eduardo José Ferreira dos Santos  
Praceta Prof. Mota Pinto  
3000-075 Coimbra, Portugal  
ejf.santos87@gmail.com

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## INTRODUCTION

Inclusion of a Central Venous Catheter (CVC) is often necessary when the clinical condition of the patient requires monitoring of some hemodynamic parameters, fluid therapy, administration of drugs, blood products, parenteral nutrition, and dialysis, among other procedures<sup>(1)</sup>. Although on the one hand its use has enabled therapeutic advances, it has also led to the origin of various associated risks, of which infection and catheter obstruction<sup>(1-4)</sup> can be highlighted; factors contributing to an increase of hospital internalizations, morbidity and hospitalization costs<sup>(4)</sup>.

For these reasons, CVC handling, maintenance and optimization is complicit to the predominant value of care, where nurses must gather a body of knowledge and skills to ensure proper handling of the CVC<sup>(5)</sup>.

Nevertheless, despite the existence of several international recommendations and *guidelines* related to this subject, doubts still persist regarding which should be used when we discuss the recommended solution to maintaining CVC patency, since there are several practices in use in the clinical setting (saline, heparin, sodium citrate, and other chemical solutions)<sup>(6)</sup>.

Historically, heparin solution has been the most commonly used method to maintain catheter patency, dating back to the 1970s<sup>(1)</sup>. However, this practice seems to have concealed its negative effects<sup>(1,3)</sup>, of which we can highlight the iatrogenic effects of the drug itself, such as thrombocytopenia.

Heparin is an anticoagulant that acts at the level of the coagulation cascade and inhibits platelet aggregation<sup>(1)</sup>, contributing to the occurrence of thrombocytopenia and bleeding, even when used in small quantities in CVC optimization (washing/*flushing*)<sup>(1,7)</sup>. It is administered daily in hospitals to approximately 12 million patients, for whom there are documented cases of morbidity and mortality associated with severe complications<sup>(7)</sup>. Thrombocytopenia associated with the administration of heparin is developed in about 1-5% of the exposed population, and it is recognized that intravenous exposure to heparin alone is a predictive factor for developing thrombocytopenia<sup>(7-8)</sup>.

From a macro perspective, indiscriminate use of heparin for CVC also has negative economic and social consequences when compared with the use of saline solution, because the obstruction of CVC implies an interruption of therapeutic treatments and an increase in the risks associated with catheterization for the patient, which becomes more important in the aspect of quality healthcare<sup>(3)</sup>.

We cannot help but reflect on the different focuses that are necessary in this practice of nursing: thrombocytopenia is related to the frequent use of heparin; thrombocytopenia risk exists even when the exposure is minimal; heparin is found in various concentrations and formulations, increasing the risk of error in dilution preparation; and several studies have suggested that heparin is related to medication errors<sup>(1,3)</sup>.

On the other hand, some studies suggest that saline *flush* is cost-effective, adequate and also has the benefit of not having the adverse effects of heparin and not having several presentations nor preparation required at different

concentrations<sup>(2,9-14)</sup>. In this context, some published studies have reported that most nurses use only saline solutions, enhancing the fact that CVC *flushing* practices vary widely, and are currently inconsistent<sup>(15)</sup>.

This fact is even more significant because most existing guidelines for maintaining CVC are not based on evidence and do not identify any recommendations that promote *flushing* with only saline solution<sup>(16)</sup>. When considering these gaps, this issue was identified as a research priority that could indicate significant benefits for the reduction of adverse events<sup>(5)</sup>. In this context, it is clear that there exists the need to investigate the decision of using heparin or 0.9% sodium chloride in CVC permeability/patency; this led us to develop the research question: *What is the most effective flush to reduce central venous catheter occlusion rates in adults?* In order to set the limits of the research, the objective was defined as: *Determining the effectiveness of heparinized flush solutions compared to 0.9% saline flush in the permeability of central venous catheters in adults.*

## METHOD

To carry out this systematic literature review and to respond to the previously formulated research question, we adopted the principles proposed by the *Cochrane Handbook*<sup>(17)</sup> and the research results were reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement<sup>(18-19)</sup>.

It is worth mentioning that prior to the start of the empirical phase of the established research process, it had been approved by Ethics Committee of the Escola Superior de Saúde de Viseu (Number 35/2013). The lead author and co-authors established the protocol for this review which has not been published.

The location and selection of studies were based on a process consisting of three stages:

- 1) An initial naturalistic research limited to MEDLINE and CINAHL was performed, followed by an analysis of the words in the titles, abstracts and indexing terms used to describe the studies. Then we decided to confirm if the preliminary terms constituted MeSH descriptors via the website <http://www.ncbi.nlm.nih.gov/mesh>, obtaining positive response for: #1 MeSH descriptor "Catheterization, central venous" (explode all trees); #2 MeSH descriptor "Catheterization" (explode all trees); #3 MeSH descriptor "Catheters" (explode all trees); #4 MeSH descriptor "Heparin" (explode all trees); #5 MeSH descriptor "Sodium chloride" (explode all trees).
- 2) The second research was carried out between December 2013 and February 2014, replicated in May 2015, and included electronic research in the following databases: CINAHL Plus with Full Text, MedicLatina, MEDLINE with Full Text, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Nursing & Allied Health Collection: Comprehensive (via EBSCO); Elsevier – Science Direct (via b-on – Online Knowledge Library); JBI Library; Scopus; Scielo – Scientific Electronic Library Online; Academic Google (for extracting full text articles that could not be

obtained by other means) – through Boolean combination of all identified keywords: #6 [#1 OR #2 OR #3 AND #4 AND #5] (subject); #7 [central venous catheter\* OR catheter\*AND heparin OR sodium chloride] (title and abstract).

- 3) Finally, the list of references of all identified studies was analyzed to extract additional studies.

#### Inclusion criteria:

**Participants:** patients with central venous catheters (of any kind). Adults aged 18 or older in the hospital and/or clinical setting. Exclusion criteria included patients with coagulation disorders, hemorrhagic disease, family history of heparin allergy, who had prolonged oral or systemic treatment with anticoagulant drugs; and patients indicated for abdominal or orthopedic surgery.

**Intervention:** studies comparing the effectiveness of different washing solutions (*flush*) to maintain the permeability of different types of central venous catheters;

**Comparisons:** all heparinized solutions described in the literature *vs.* 0.9% saline solution;

**Outcome:** *CVC occlusion rate* (defined as inability to infuse fluid through the catheter due to an obstruction);

**Design:** only experimental studies were included, including randomized controlled trials, non-randomized controlled studies; and quasi-experimental studies, including *before-and-after* studies and cohort studies; studies published in English, Spanish and Portuguese; published from January 2000 to May 2015.

A critical appraisal was done prior to inclusion in the review by two reviewers with experience in the isolated method, and neither had knowledge of test results at any time during this process<sup>(17)</sup>.

The tools for critical appraisal were: *Grid for critical evaluation of an article describing a prospective, randomized and controlled clinical study* of the Centro de Estudos de Medicina Baseada na Evidência da Faculdade de Medicina de Lisboa, Portugal, which only considers *high-quality* studies which met a score equal to or higher than 75%<sup>(20)</sup> to assess RCT (Randomized Clinical Trial); and *JBIC Critical Appraisal Checklist for Cohort and Case-Control Studies* that according to the consensus of the authors are considered quality studies that obtain up to two negative responses<sup>(21-22)</sup> to assess cohort studies. In the absence of consensus among the reviewers, disagreements that emerged were resolved through discussion with the inclusion of a third reviewer<sup>(22)</sup>.

Data were extracted from the included studies in the corpus by two isolated reviewers using the instrument *The Joanna Briggs Institute data extraction form for systematic review of experimental/observational studies*, with disagreements being resolved by discussion or a third reviewer. The authors were contacted for information or missing data that needed clarification<sup>(22)</sup>.

In the process of synthesis, quantitative data were grouped and meta-analysis was performed with the use of Cochrane Collaboration's Review Manager software (RevMan 5.2.8; <<http://ims.cochrane.org/RevMan>>). All results were subjected to dual input data.

The results were expressed in relative risk (RR) with 95% confidence intervals, as referring to dichotomous data (categorical data).

The *Q* test and *I*<sup>2</sup> were calculated to verify the existence of heterogeneity among studies, where a *I*<sup>2</sup> value close to 0% indicates no heterogeneity, close to 25% indicates low heterogeneity, close to 50% indicates moderate heterogeneity, and close to 75% indicates high heterogeneity among the studies<sup>(23)</sup>. Due to the heterogeneity found, analyses were performed with the use of the random effects model<sup>(21-23)</sup>, which implies that the effect of interest is not the same across all the studies, assuming the existence of a certain degree of clinical heterogeneity that is not liable to be controlled<sup>(23)</sup>.

Levels of evidence and grades of recommendation were established based on the classification currently used<sup>(24)</sup>.

Effectiveness comparison of heparinized *flush* solutions with 0.9% saline *flush* on CVC permeability was performed through three analyses (meta-analysis by subgroups): by CVC type, by design of the included studies and by their *setting* (context).

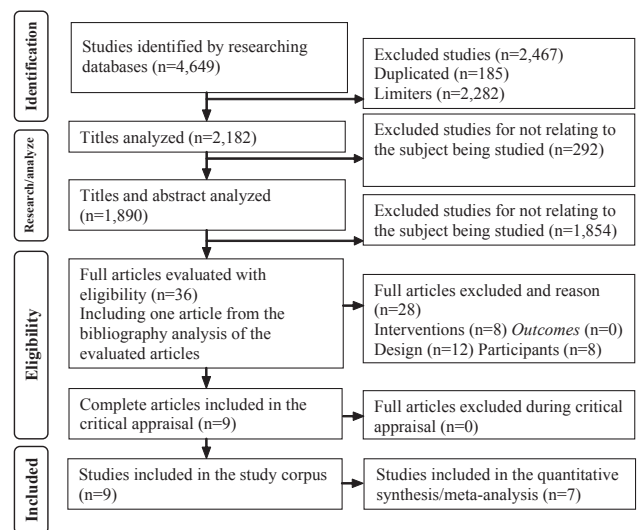
## RESULTS

Of all the studies identified by the method explained in the previous section, we noted that the first selected sample comprised 4,649 studies.

Two independent researchers excluded 292 studies based on the inclusion criteria by reading the titles and 1,854 by reading the abstract.

After analyzing the full text of the articles (n=36), 28 studies were excluded, resulting in a *corpus* consisting of eight studies. Bibliography analysis of identified reference articles also allowed the inclusion of another study, thus nine studies were considered for critical appraisal: eight RCT<sup>(2,6,9,11-14,16)</sup> and one cohort study<sup>(10)</sup>.

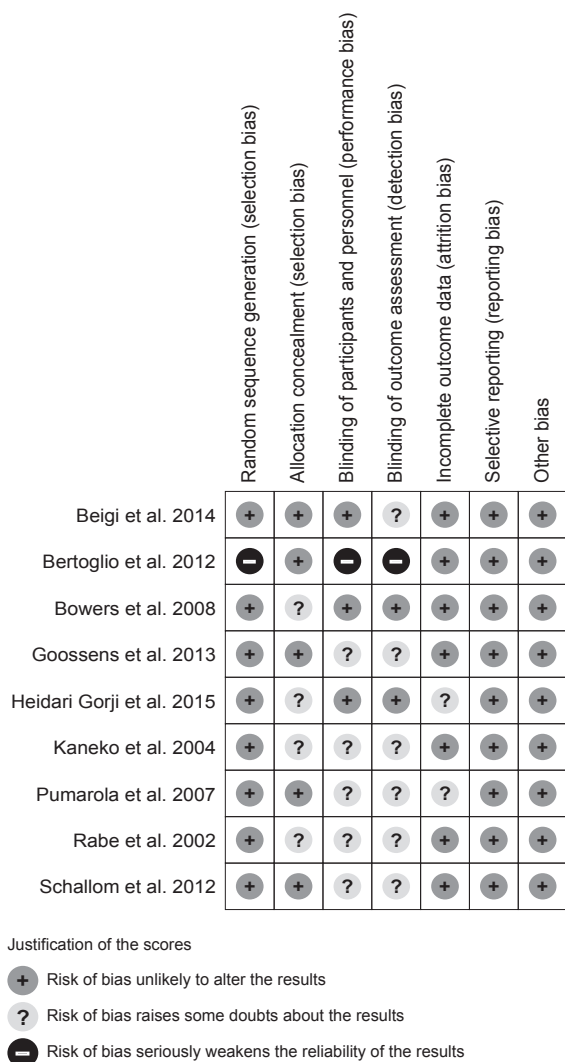
The entire process of study *corpus* selection can be summarized by the following flow chart (shown in Figure 1).



**Figure 1** – Representative flowchart of study corpus refinement stages – Viseu, Portugal, 2015.

For a detailed explanation of the evaluation of the methodological quality of the studies, we present Figure 2

based on the “Cochrane Collaboration tool for Assessing risk of bias”<sup>(17)</sup>.



**Figure 2** – Summary of risk of bias according to the critical appraisal of the reviewers – Viseu, Portugal, 2015.

Below we present a summary of the most important aspects of the characteristics of the studies included in the study corpus, which were grouped and organized into an “evidence table” (see Chart 1).

**Chart 1** – Study corpus characteristics of the included studies – Viseu, Portugal, 2015.

| Study                        | CVC specificities               | Evaluation of catheter permeability | Catheters duration/ time | Type of infusion (medicinal products and solutions) |
|------------------------------|---------------------------------|-------------------------------------|--------------------------|---|
| Rabe et al. <sup>(6)</sup>   | Triple-Lumen CVC                | Every 2 days                        | 20 days                  | Not reported  |
| Kaneko et al. <sup>(9)</sup> | Double-Lumen CVC with urokinase | After each hemodialysis session     | Not reported             | Hemodialysis  |

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| Study                                | CVC specificities         | Evaluation of catheter permeability   | Catheters duration/ time                      | Type of infusion (medicinal products and solutions)   |
|--------------------------------------|---------------------------|---|---|---|
| Pumarola et al. <sup>(2)</sup>       | Triple-Lumen CVC          | At 24 and 72 hours, and at hospital discharge   | Until catheter occlusion or medical discharge | Not reported  |
| Bertoglio et al. <sup>(10)</sup>     | Fully deployed CVC        | Monthly evaluation or at the end of each therapeutic administration   | Minimum of 12 months                          | Chemotherapy; Parenteral nutrition  |
| Schallom et al. <sup>(11)</sup>      | Multiple-Lumen CVC        | Every 8 hours, intravenous without continuous infusion  | 22 days                                       | Intermittent and non-specific continuous infusions  |
| Goossens et al. <sup>(12)</sup>      | Fully deployed CVC        | Before removing the needle from the CVC; before and after each therapy administration and every 8 weeks if not in use | 180 days                                      | Intermittent and non-specific continuous infusions; Blood derivatives; Parenteral nutrition |
| Bowers et al. <sup>(13)</sup>        | Peripherally inserted CVC | According to medical prescription, at every 12 or 24 hours  | Until catheter occlusion or medical discharge | Non-specific intravenous therapy  |
| Heidari Gorji et al. <sup>(16)</sup> | CVC                       | Every 8 hours, intravenous without continuous infusion  | 21 days                                       | Non-specific intravenous therapy  |
| Beigi et al. <sup>(14)</sup>         | Double-Lumen CVC          | At CVC placement, at 12 and 24 hours  | 1 day   | Hemodialysis  |

We also present a summary of the most important aspects of the main results from analyzing the selected studies (see Chart 2).

**SUMMARY OF QUANTITATIVE DATA - META-ANALYSIS**

Analyzing the results of the meta-analysis and the respective *forest plot* (as shown in Figure 3), we can infer that there is no statistical significance, because the combined result of the meta-analysis overlaps the no-effect line.

Nevertheless, we can still point out that there is a beneficial effect in the group using the heparinized solutions as a *flush* because although there is no statistical significance, there is increased risk of non-permeable CVC in the saline solution group, supported by the value of meta-analytical result (RR=0.68, CI 95%=0.41-1.10; *p*=0.12). From the heterogeneity study we can infer that this is statistically significant and it is classified as low (Tau<sup>2</sup>=0.03,  $\chi^2$ =4.41, *df*=4, *p*=0.35; *I*<sup>2</sup>=9%).

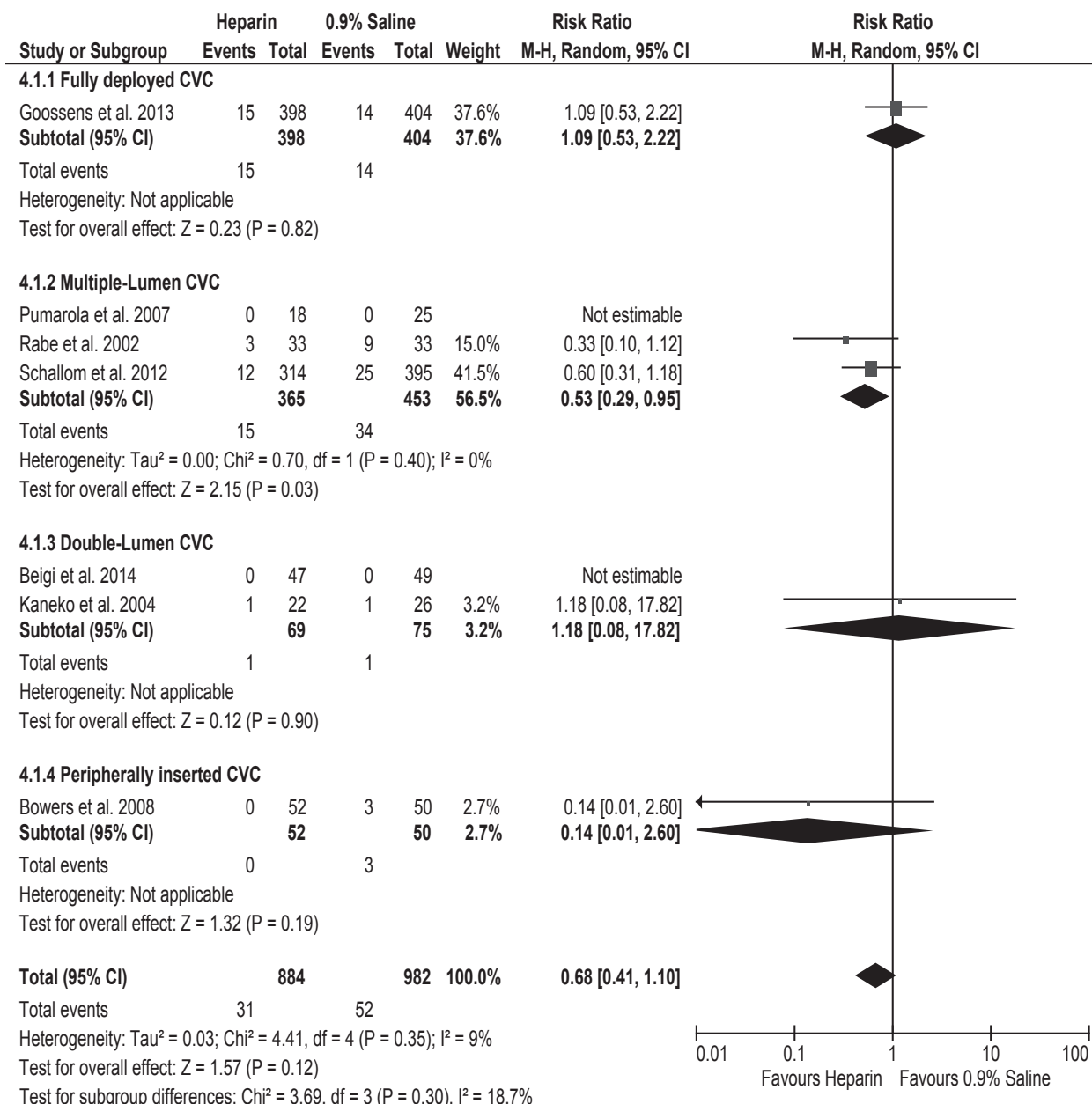
For the subgroup of fully deployed CVC, it was found that there are no statistically significant differences

(RR=1.09, CI 95%=0.53-2.22;  $p=0.82$ ). In the subgroup of CVC with multiple lumens, there was a beneficial effect in the heparin group, which is a statistically significant result (RR=0.53, CI 95%=0.29-0.95;  $p=0.03$ ) and without significant heterogeneity among the studies (Tau<sup>2</sup>=0.00;  $\chi^2=0.70$ , df=1,  $p=0.40$ ;  $I^2=0\%$ ). In the subgroup of double lumen CVC for hemodialysis, a beneficial effect in the saline solution

group was verified, although it did not reach statistical significance (RR=1.18, CI 95%=0.08-17.82;  $p=0.90$ ). Finally, in relation to the subgroup of peripherally inserted CVC, statistical significance was also not observed (RR=0.14, CI 95%=0.01-2.60;  $p=0.19$ ). We emphasize that the analysis of the differences between subgroups reveals low heterogeneity ( $\chi^2=3.69$ , df=3,  $p=0.30$ ;  $I^2=18.7\%$ ).

**Chart 2** – Main results of the studies included in the study corpus – Viseu, Portugal, 2015

| Author/ Year/ Country                          | Type of study/ Population   | Interventions                         |   | Results/Outcomes   | Conclusions  | Critical appraisal of quality |
|--|---|---------------------------------------|---|--|--|-------------------------------|
|  |   | Experimental                          | Control   |  |  |                               |
| Rabe et al. <sup>(6)</sup><br>(Germany)        | RCT/n = 99<br>Participants in intensive care                          | 5000IU of Heparin/ml <i>Flush</i>     | 0.9% saline solution <i>Flush</i><br>200 mg/ml vitamin C <i>Flush</i> | There was no difference between the use of heparin and the SS ( $p < 0.04$ , log-rank test).             | Heparin-solutions are most effective when compared to saline solution in maintaining CVC permeability.         | 80%                           |
| Kaneko et al. <sup>(9)</sup><br>(Japan)        | RCT/n = 48<br>Hospitalized participants                               | 20 ml of saline solution <i>Flush</i> | 20 ml of saline solution <i>Flush</i> + 2 ml of 1000 IU/ml heparin    | There was no difference between the use of heparin and the SS ( $p = 0.8599$ ).                          | Saline solution is sufficient in maintaining central catheter permeability for hemodialysis.                   | 75%                           |
| Pumarola et al. <sup>(2)</sup><br>(Spain)      | RCT/n = 95<br>Participants in intensive care                          | 0.9% saline solution <i>Flush</i>     | 100IU Heparin <i>Flush</i>  | There was no difference between the use of heparin and SS ( $p = 0.744$ ).                               | 0.9% saline is also effective compared to 100 IU or 500 IU heparin in maintaining CVC permeability.            | 85%                           |
| Bertoglio et al. <sup>(10)</sup><br>(Italy)    | Retrospective cohort study/n = 610<br>Participants in the cancer unit | 500 IU/ SS 10 ml Heparin <i>Flush</i> | 10 ml of 0.9% saline solution <i>Flush</i>                            | There was no difference between the use of heparin and SS (HR -1.2; 95% CI: 0.6-2.5; $p = 0.7$ ).        | Saline solution is as effective as heparinized solution in maintaining patency.                                | 7 points                      |
| Schallom et al. <sup>(11)</sup><br>(USA)       | RCT/n = 709<br>lumens/n = 341<br>Hospitalized participants            | 10IU Heparin/ml <i>Flush</i>          | 10 ml of 0.9% saline solution <i>Flush</i>                            | There was no difference between the use of heparin and SS (RR = 1.66, 95% CI = 0.86-3.22; $p = 0.136$ ). | Saline solution may be preferable in maintaining CVC patency, when used for a short time, compared to heparin. | 85%                           |
| Goossens et al. <sup>(12)</sup><br>(Belgium)   | RCT/n = 802<br>Participants of the cancer unit                        | 300IU Heparin /3ml <i>Flush</i>       | 10 ml of 0.9% saline solution <i>Flush</i>                            | There was no difference between the use of heparin and SS (RR = 0.94, 95% CI = 0.67%-1.32%).             | Saline is an effective solution for fully deployed CVC <i>flush</i> .  | 85%                           |
| Bowers et al. <sup>(13)</sup>                  | RCT/n = 102<br>Hospitalized participants                              | 100 IU/ml (3 ml) Heparin <i>Flush</i> | 10 ml of 0.9% saline solution <i>Flush</i>                            | There was no difference between the use of heparin and SS (6% rates of occlusion in SS group).           | Saline solution is sufficient in maintaining CVC permeability of peripheral insertions.                        | 80%                           |
| Heidari Gorji et al. <sup>(16)</sup><br>(Iran) | RCT/n = 84<br>Participants in intensive care                          | 10 IU/ml (3 ml) Heparin <i>Flush</i>  | 10 ml of 0.9% saline solution <i>Flush</i>                            | There was no difference between the use of heparin and SS ( $p = 0.872$ ).                               | Saline solution is recommended in maintaining CVC permeability.  | 85%                           |
| Beigi et al. <sup>(14)</sup><br>(Iran)         | RCT/n = 96<br>Hospitalized participants                               | 1000 IU/10 ml SS Heparin <i>Flush</i> | 10 ml of 0.9% saline solution <i>Flush</i>                            | There was no difference between the use of heparin and SS (no CVC occlusions)                            | Saline is effective in maintaining CVC permeability for hemodialysis.  | 80%                           |



**Figure 3** - Forest plot of heparin comparison versus saline solution for CVC permeability from RCT studies for the outcome of non-permeable CVC for subgroups of CVC types – Visau, Portugal, 2015.

## DISCUSSION

First, we must mention that to have adopted strict selection criteria and rigidly followed every step of conducting a systematic review, we consider valid, reliable and transferable results. Yet we cannot help but notice that in some of the included studies researchers did not practice blinding, and yet there were some particular aspects of the allocation, randomization and incomplete data that were not met.

The heterogeneity found by statistical analysis is probably due to the difference between the methodological quality of the included RCT (methodological heterogeneity), the fact that they do not possess wholly similar interventions such as different dilutions of heparin solutions, the different types of CVC, and also because the populations

have different pathology (clinical heterogeneity). We also acknowledge that the non-permeable definition of CVC is different between the included studies, which may possibly translate some level of statistical heterogeneity<sup>(11)</sup>. Nevertheless, by assuming the existence of these heterogeneities, by carrying out analyzes of subgroups and fulfilling all the recommendations, we believe that this fact does not limit our conclusions.

We therefore observed that heparin CVC has been considered over the years as a traditional and useful practice in maintaining the permeability of CVC, however this practice remains shrouded in some controversy. Heparin by itself is not a thrombolytic agent, it does not cause lysis or clot “fragmentation,” but prevents the progression of previously existing clots by inhibiting the factors related to the process

of clot formation, allowing lysis of the naturally occurring clot. Moreover, heparin has a very short lifespan (60 to 90 min) and no data or evidence present perfect validity of the dilution and therapeutic components of CVC to meet the therapeutic effect on one hand, and on the other and even more critically do not produce its undesirable side effects<sup>(10)</sup>.

Moreover, there is no evidence in the literature that the concentration of heparin alone is related to improved permeable CVC rates, assuming a balance between effectiveness and safety of the patient<sup>(10)</sup>. However, the systemic effects of the use of heparin and the development of heparin-induced thrombocytopenia may constitute a problem<sup>(6)</sup>.

Despite the potential benefits of saline solution, the change in clinical practice for a normal saline solution has not been widely suggested in the literature for the whole typology of patients and CVC. A possible explanation for this may be attributed to the long period of time that CVC remains in the patient<sup>(25-27)</sup>, complications associated with maintaining CVC<sup>(28-31)</sup>, type of infusion used (medicinal, solutions...)<sup>(32)</sup>; if the purpose of the CVC is hemodialysis<sup>(9-14)</sup> and institutional procedures for *locking and flushing* can strengthen medical belief about heparin effectiveness<sup>(10)</sup>, thus ultimately leading to exploiting the effectiveness of other solutions<sup>(33)</sup> (i.e. citrate).

Although most of the study's corpus suggest the use of saline solution, one study<sup>(6)</sup> concluded that heparinized solutions are more effective when compared to saline solution for maintaining CVC patency. It is important to note that the *flush* technique has not been described in detail and it was performed only every 48 hours, which may have contributed to the differences, for example, in comparing this procedure to the study<sup>(11)</sup> in which the *flush* technique has been described in detail and implemented every 8 hours. The same authors also point out that the strength of the results is due to adopting protocol operations and a higher nurse/patient ratio, so the standardization of practices for conducting a *flush* every 8 hours, and the criteria for the administrative *flush* order according to the intravenous therapy (treatments) and interventions are shown as vital procedures.

In defense of the determined evidence, it is also noteworthy that our meta-analysis results indicate that there is no statistically significant difference between the efficacies of *flush* solutions, which is supported by the value of meta-analytic results (RR=0.68, CI 95%=0.41-1.10;  $p=0.12$ ). These results clearly show that implementing the saline solution *flush* in maintaining patency of CVC must be transferred to clinical practice.

In short, we should mention that the consensus among various authors and our results are consistent, allowing us to

draw the following conclusions: the saline solution is sufficient for maintaining patency of CVC when compared to heparinized solutions<sup>(2,9-14,16)</sup>; saline solution prevents exposure to complications arising from the use of heparin – these being thrombocytopenia, bleeding<sup>(11,12,14,16)</sup>... thereby adding significance when associated with differences in the dilutions used (often by the team itself), non-uniformity of pre-established protocols and potential errors of medication preparation<sup>(1)</sup>.

## CONCLUSION

Currently, CVC obstruction is assumed as an important concern for health professionals because it implies the suspension of therapies, an increase risk to the patient and associated costs. In this sense, strategies to reduce this complication are crucial, in particular the choice of solution being used to maintain CVC patency.

According to available evidence, the consensus among several authors and the results of this systematic review show no significant differences between the effectiveness of heparinized solutions and saline 0.9% in maintaining CVC patency in adults (RR=0.68, CI 95%=0.41-1.10;  $p=0.12$ ).

Considering that there is evidence that using saline solution is sufficient for maintaining CVC patency, thus preventing the risks associated with the administration of heparin, we suggest the realization and implementation of a new *guideline*; with the main purpose being better resource management, making the technique related to the issue of general research for all health professionals.

## PRACTICAL IMPLICATIONS

The interventions considered in this systematic review are effective and can be useful in practice (Level of Evidence 1.b); health care professionals can use these interventions on adults (Grade A recommendation).

## RESEARCH IMPLICATIONS

It is necessary to properly carry out RCT designed to compare the clinical benefits, economic evaluations, patient safety and cost-effectiveness of solutions in different groups of patients (comorbidities), different types of CVC, CVC insertion reasons (intravenous therapy, parenteral nutrition, chemotherapy ...), according to the estimated time (short or long term) and covering other *outcomes* for establishing causal relationships (in addition to the number of non-permeable CVC).

RCT that validate the application of a performance protocol are necessary to maintain CVC permeability by using 0.9% saline *flush* and that prove the effectiveness of different techniques.

## RESUMO

**Objetivo:** Determinar qual é a solução (*flush* heparina comparado com o *flush* de soro fisiológico 0.9%) mais eficaz na redução do risco de oclusões de cateteres venosos centrais (CVC) em adultos. **Método:** A revisão sistemática seguiu os princípios propostos pelo *Cochrane Handbook*; a análise crítica, a extração e a síntese dos dados foram realizadas por dois investigadores, isoladamente; e a análise estatística efetuada com recurso ao programa RevMan 5.2.8. **Resultados:** Foram incluídos oito estudos randomizados controlados e um estudo de

coorte e os resultados da meta-análise mostram não existir diferenças (RR=0.68, IC 95%=0.41-1.10;  $p=0.12$ ). A análise por subgrupos mostra que nos CVC totalmente implantados não se verificaram diferenças (RR=1.09, IC 95%=0.53-2.22;  $p=0.82$ ); nos CVC com vários lúmens existiu um efeito benéfico no grupo da heparina (RR=0.53, IC 95%=0.29-0.95;  $p=0.03$ ); nos CVC de duplo lúmen para hemodiálise (RR=1.18, IC 95%=0.08-17.82;  $p=0.90$ ) e nos CVC de inserção periférica (RR=0.14, IC 95%=0.01-2.60;  $p=0.19$ ) também não se verificaram diferenças. **Conclusão:** O soro fisiológico é suficiente para manter a permeabilidade dos cateteres venosos centrais, prevenindo os riscos associados à administração da heparina.

## DESCRITORES

Cateterismo Venoso Central; Heparina; Cloreto de Sódio; Cateteres Venosos Centrais; Revisão.

## RESUMEN

**Objetivo:** Determinar cuál es la solución (*flush* con heparina comparado con el de suero fisiológico al 0,9%) más eficaz en la reducción del riesgo de oclusiones de catéteres venosos centrales (CVC) en adultos. **Método:** La revisión sistemática siguió los principios propuestos por el *Cochrane Handbook*; el análisis crítico, la extracción y la síntesis de los datos fueron realizados por dos investigadores, aisladamente; y el análisis estadístico fue llevado a cabo con recurso al programa RevMan 5.2.8. **Resultados:** Se incluyeron ocho estudios randomizados controlados y un estudio de cohorte, y los resultados del metaanálisis muestran no existir diferencias (RR=0.68, IC 95%=0.41-1.10;  $p=0.12$ ). El análisis por subgrupos muestra que en los CVC totalmente implantados no se verificaron diferencias (RR=1.09, IC 95%=0.53-2.22;  $p=0.82$ ); en los CVC con varios lúmenes existió un efecto benéfico en el grupo de la heparina (RR=0.53, IC 95%=0.29-0.95;  $p=0.03$ ); en los CVC de doble lumen para hemodiálisis (RR=1.18, IC 95%=0.08-17.82;  $p=0.90$ ) y en los CVC de inserción periférica (RR=0.14, IC 95%=0.01-2.60;  $p=0.19$ ) tampoco se verificaron diferencias. **Conclusión:** El suero fisiológico es suficiente para mantener la permeabilidad de los catéteres venosos centrales, previniendo los riesgos asociados con la administración de la heparina.

## DESCRIPTORES

Cateterismo Venoso Central; Heparina; Cloruro de Sodio; Catéteres Venosos Centrales; Revisión.

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