



## Letter to the Editors-in-Chief

## Prevalence of venous thromboembolism following head and neck cancer surgery: A systematic review and meta-analysis



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## 1. Introduction

Venous thromboembolism (VTE) is a severe complication related to cancer surgery [1]. Head and neck cancer surgical procedures combine tumour resection and neck dissection with reconstructive surgery if necessary. Hence, several risk factors for VTE are accumulated such as general anaesthesia, prolonged operation time, immobilisation, and cancer surgery [1].

Current guidelines recommend thromboprophylaxis with low-molecular-weight heparins in cancer surgery [2]. However, compliance with thromboprophylaxis guidelines varies in head and neck cancer surgery [3].

Recently, a meta-analysis investigating thromboprophylaxis in major head and neck surgery found an overall VTE prevalence of 0.9% in a mixed population of both cancer and non-cancer patients [4]. However, the prevalence might be higher in cohorts consisting of head and neck cancer patients exclusively. Hence, the aim of this study was to systematically review the literature on VTE-prevalence following head and neck cancer surgery and estimate the overall prevalence in a meta-analysis. Secondary, to clarify current thromboprophylaxis regimens.

## 2. Methods

## 2.1. Search strategy

This systematic review was conducted according to the PRISMA statement. PubMed and Embase databases were searched on February 16, 2017. The PubMed search terms were: (“embolism and thrombosis”[Mesh] or “deep vein thrombosis” or “DVT” or “pulmonary embolism”) and (“head and neck neoplasms”[Mesh]) and (“surgery”). The Embase search terms were: ((‘thromboembolism’/exp OR ‘dvt’ OR ‘deep venous thrombosis’ OR ‘pulmonary embolism’) AND (‘head and neck tumor’/exp OR ‘epiglottis tumor’/exp OR ‘larynx tumor’/exp OR ‘nose tumor’/exp) AND ‘surgery’). Search filters were applied to remove non-English records, non-human records, and reviews in the databases. Furthermore, additional records were found in the reference list of identified studies.

## 2.2. Study selection

Eligibility criteria were pre-specified in a search protocol before the initial literature search. The inclusion criteria were: 1) original articles or meta-analyses of human trials; 2) including patients undergoing head and neck cancer surgery; and 3) with diagnosis of VTE either intra- or postoperatively. Cervical oesophageal cancer was included as a head and neck cancer. Exclusion criteria were: 1) studies in which only biochemical markers were investigated; 2) thrombosis located to the anastomoses in microvascular reconstructive surgery; 3) superficial vein thrombosis; 4) pure cohorts with resection of skin cancer or malignant melanoma located in the head and neck region; 5) non-English language publications; 6) reviews, guidelines, case reports with less than five cases, editorials, conference abstracts and papers, and letters and comments without original data; 7) animal studies; and 8) *in vitro* studies.

The study selection strategy was tested based on a sample of 100 random abstracts, and consensus was reached between all authors. Hereafter, one author (M.L.) performed study screening, selection, and data extraction. All records were initially screened by title and abstract. Studies considered relevant were assessed in full-text and evaluated owing to the eligibility criteria.

## 2.3. Statistical analysis

Data were extracted from the included studies for calculation of the VTE prevalence for each study. The extracted prevalence proportions were transformed by the double arcsine model to calculate a mean estimate with 95% confidence intervals [5]. A fixed effects model was chosen to incorporate within study variance and difference in sample size thereby calculating an overall prevalence [5].  $I^2$  statistic was performed to assess the heterogeneity among the included studies [5]. The statistical analyses were performed in Meta-XL (EpiGear International, Sunrise Beach, Queensland, Australia) and presented in a forest plot.

## 3. Results

Fig. 1 shows the article inclusion and exclusion process. In total,

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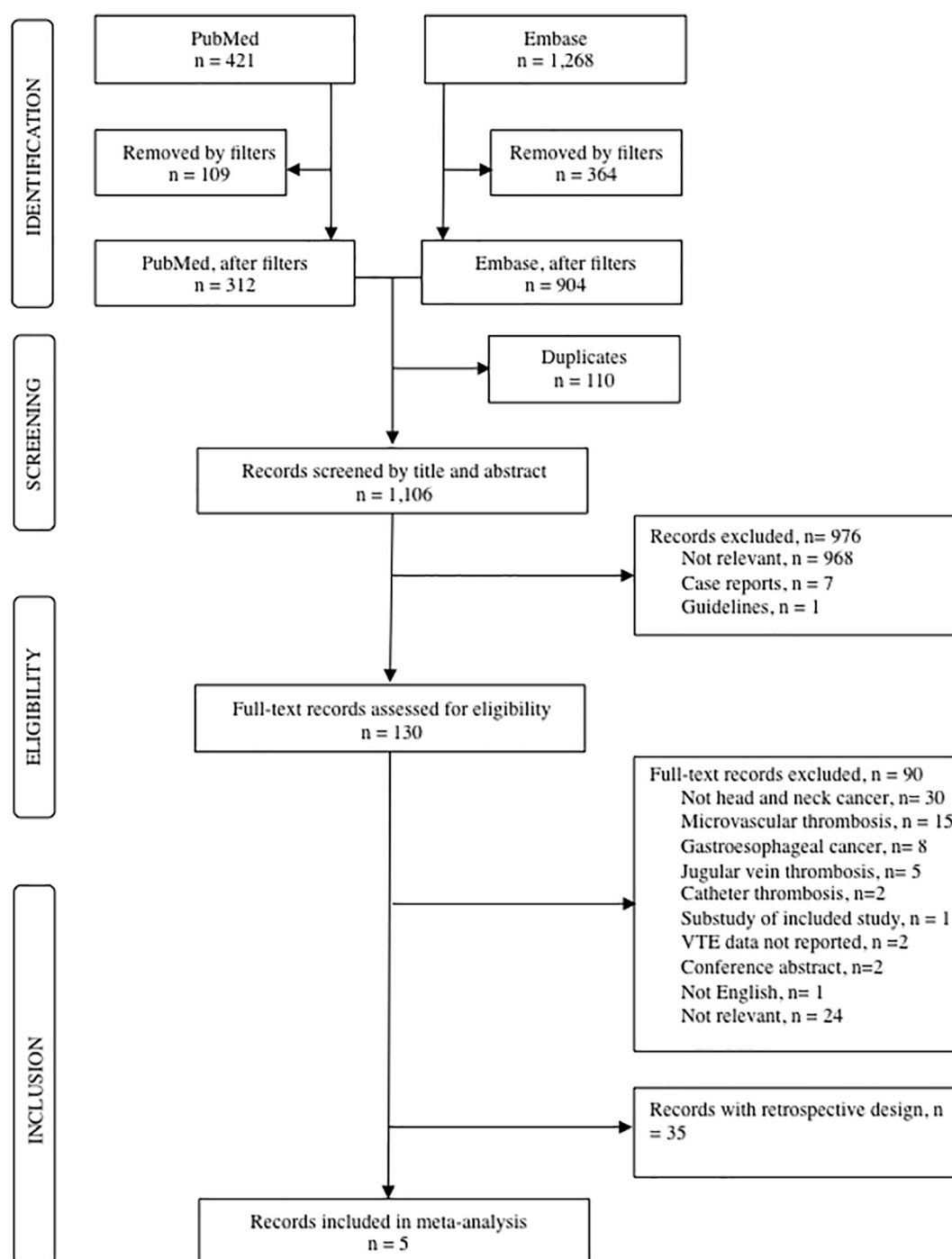


Fig. 1. Flow diagram of the publication inclusion and exclusion process.

1689 records were identified. Thereafter, 473 records were removed by filters and 110 were duplicates. Thus, 1106 records were screened by title and abstract. Among these, 976 were excluded. In total, 130 full-text records were assessed for eligibility. Of these, 90 were excluded in accordance with the exclusion criteria as shown in Fig. 1. In addition, 35 retrospective records met the inclusion criteria. However, these were excluded due to high heterogeneity. Thus, five prospective studies were included in the systematic review and meta-analysis.

The five prospective studies are presented in Table 1. All studies were cohort studies [6–10].

The patients' mean age was reported in four studies ranging from 56 to 63 years mean or median years [6,7,9,10]. The most common histology type was squamous cell carcinoma [6,7,10]. One study reported

use of preoperative chemotherapy [10]. The main surgical procedure was tumour resection combined with either neck dissection, microvascular reconstruction or both [6–10]. Three studies reported a mean operation duration ranging from 1.9 to 7.2 h [6–8]. Two studies reported a follow-up period from 30 to 90 days [6,10]. Three studies did not report the follow-up period [7–9].

Fig. 2 shows a forest plot of the prevalence proportion of all the prospective studies [6–10]. The overall pooled VTE prevalence was 5% (95% confidence interval: 1–11%) and the overall  $I^2$  coefficient was 41% (95% confidence interval: 0–78%).

Two studies administered pharmacological thromboprophylaxis by low-molecular-weight heparin and reported a VTE prevalence of 0% [8,9]. In the study by Clayburgh et al., mechanical thromboprophylaxis

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