Postoperative sore throat and hoarseness
To my beloved family

Life is like riding a bicycle.  
To keep your balance you must keep moving.  
Albert Einstein
Postoperative sore throat and hoarseness
Clinical studies in patients undergoing general anesthesia
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Abstract


A common problem following general anesthesia is postoperative sore throat (POST) and postoperative hoarseness (PH). Symptoms directly correlated with less satisfaction according to the patients. The overall aim of this thesis was to describe patients' postoperative sore throat and hoarseness after general anesthesia with endotracheal intubation or laryngeal mask airway. As well as to investigate the risk factors that are associated with the symptoms, and to test methods that may prevent sore throat and hoarseness after a general anaesthetics. A total of 889 patients are included in the four studies. Incidence of POST varied from 21% up to 52% depending on endotracheal tube (ETT) size in women (I-IV) and in men was the incidence 32-38% (III-IV). There were no gender difference in POST in study III and IV. The overall incidence of PH varied from 42-59% (I-IV) in all patients, with no gender differences (III-IV). Following a laryngeal mask airway (LMA) 19% of the patients had POST and 33% of the patients reported PH. Patients with POST do seem to be able to localize their pain in the throat (IV). Different risk factors are shown to contribute to both POST and PH in men and women (II-III). To intubate with a smaller ETT size, 6.0 vs. 7.0 decreased POST in women in the early postoperative period as well as their discomfort from their POST (I). Only 6% of men who needed a laryngeal mask airway had POST compared to 26% of women. The symptoms are more discomforting after an ETT vs. an LMA up to 24 hours (IV). More patients have sore throat and hoarseness in the early postoperative period, but the symptoms can remain up to almost 5 days postoperatively (I, IV). In summary, sore throat and hoarseness following general anesthesia, affects many patients postoperatively. To intubate women with endotracheal size 6.0 decreases both sore throat and hoarseness postoperatively. Women are more likely than men to have a sore throat when a laryngeal mask airway is used.

Keywords: Sore throat, Hoarseness, Postoperative, Complication, Endotracheal tube, Laryngeal Mask Airway, Gender, Risk factor.

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LIST OF ABBREVIATIONS

CRF  Clinical research form
ENT  Ear, nose, and throat
ETT  Endotracheal tube
LMA  Laryngeal mask airway
HVLP High-volume low-pressure
ICU  Intensive care unit
ID   Inner diameter
IL-6 Interleukin 6
LVHP Low-volume high-pressure
MD   Medical doctor
NRS  Numeric rating scale
OR   Operating room
PACU Post-anesthesia care unit
PH   Postoperative hoarseness
PONV Postoperative nausea and vomiting
POST Postoperative sore throat
RCT  Randomized controlled trial
RNA  Registered anesthesia nurse
RN   Registered nurse
VAS  Visual analog scale

ASA Classification
ASA I Healthy person
ASA II Person with a mild systemic disease e.g. high blood pressure
ASA III Severe systemic disease
ASA IV Severe systemic disease that is a constant threat to life
ASA V A moribund person who is not expected to live without the operation
ASA VI A declared brain dead person whose organs are being removed for donor purposes

Cormack & Lehane Classification
Grade I Full view of glottis
Grade II Partial view of glottis
Grade III Only epiglottis seen, none of glottis seen
Grade IV Neither glottis nor epiglottis seen

Mallampati Classification
Mallampati I Soft palate, uvula, fauces and pillars visible
Mallampati II Soft palate, uvula and fauces visible
Mallampati III Soft palate and base of uvula visible
Mallampati IV Only hard palate visible
LIST OF PUBLICATIONS

This thesis is based on following papers, and will be referred to in the text with their roman numerals.

I  

II  

III  

IV  
Jaensson, M., Gupta, A., & Nilsson, U. Sore throat and hoarseness following endotracheal tube or laryngeal mask airway: A prospective study Submitted

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INTRODUCTION

In my clinical work as a Registered Nurse Anesthetist (RNA), one of my most important roles is to ensure that the patients maintain a free airway during surgery. This can be done with different devices, such as an endotracheal tube (ETT) or a laryngeal mask airway (LMA). Irrespective of the device used, I have encountered many patients who complain about a sore throat on their way to the post anesthesia care unit (PACU). Additionally, many patients express surprise that their voice is different than it was before surgery. Personnel working in the PACU have also confirmed that this is a clinical problem for patients during the early postoperative period. The RNA is an advocate for the patient, and among other responsibilities, both ethical and moral\(^1\), this involves reducing the patient’s pain and discomfort and preventing complications\(^2\). This daily clinical problem consequently made me curious about how to better understand this minor but common problem, and reduce its incidence in the future. Can nurses do anything to prevent these symptoms, and are there any risk factors that may predict which patients will suffer from postoperative sore throat (POST) or postoperative hoarseness (PH)? While reviewing the literature, I discovered a variety of ways in which this problem has been tackled. It was also evident that most studies had not examined whether there were any differences between the sexes in how they experienced POST or PH.

Although the literature describes POST and PH as minor adverse events, it is important to avoid them since they are directly related to patients’ wellbeing and satisfaction with anesthesia care\(^3\).

This thesis is my contribution to knowledge about these risk factors, as well as what actions we can take during anesthesia care that may prevent patients from developing postoperative sore throat and postoperative hoarseness.
**BACKGROUND**

**Anesthesia**
Amongst others, one important aim of good anesthetic care is to achieve a secure airway and to ventilate the lungs in a proper physiological manner. This can be done in different ways, depending on the patient’s characteristics as well as the surgery itself. A safe and secure airway can be achieved by using an endotracheal tube (ETT) or using a laryngeal mask airway (LMA). Airway management can be performed by either an anesthesiologist or RNA. However, after prescription by an anesthesiologist, the RNA can plan and administer general anesthesia during elective surgery of American Society of Anesthesiologists (ASA) physical status classification I-II patients.

**Anatomy of the Airway**
The pharynx consists of three compartments: the nasopharynx, the oropharynx, and the hypopharynx. The hypopharynx starts at the epiglottis and ends at the lower end of the cricoid cartilage. The larynx consists of different cartilage including the cricoid, thyroid, and arytenoid cartilage. The vocal cords run from the arytenoid cartilage through to the posterior surface of the thyroid cartilage. The space between the vocal cords, the rima glottidis, is one of the narrowest parts of the airway, the other being at the cricoid cartilage. Women have a narrower larynx than men. The epiglottis protects the larynx from aspiration or foreign matter. When intubating with the Macintosh laryngoscope, the tip of the laryngoscope has to be placed in the vallecula and lifted, which stretches these structures. The trachea begins just below the cricoid cartilage and extends to the carina with a total length of 10-20 cm. in an adult. Several nerves supply motor and sensory fibers to the airway. The glossopharyngeal and the vagus nerve together innervate the pharynx, larynx, and soft palate. Two branches of the vagus nerve, the superior laryngeal nerve and the recurrent laryngeal nerve, innervate the hypopharynx.
The Endotracheal Tube

The ETT is made of polyvinylchloride (PVC) and has a cuff at the distal end. The cuff is a balloon whose purpose is to protect the lungs against aspiration of gastric contents, and to protect the environment in the operating room from anesthetic gases such as sevorane, desflurane, and nitrous oxide4.

In the 1980s when patients were intubated using an ETT the gold standard was an ETT, with an 8.0 inner diameter (ID) for women and a 9.0 ID for men7. Nowadays, the tubes are normally smaller-size 7.0 for women and 8.0 for men, according to textbooks4,10. However, Stout et al.11 showed that both women and men could benefit from smaller tube sizes, which can reduce their chances of suffering from POST or PH. The risk involved in using an ETT with a smaller ID can be air-trapping (auto-PEEP) and insufficient time to complete exhalation9. However, there seems to be no evidence for the latter when using ETT size 6.04. A potential problem, though, is the difficulty of performing a bronchoscopy intraoperatively through a smaller ETT12.

The appropriate ETT size in women and men is still under debate in the anesthesia community. The answer might vary depending on whether the patient is intubated in the short term, as during anesthesia and surgery, or for a longer period of time in the intensive care unit (ICU). A smaller sized ETT can make it difficult to perform bronchoscopy and to ventilate ICU patients12.
The LMA placed in the hypopharynx © Maria Bergman

The Laryngeal Mask Airway

The LMA is a plastic tube with a cuff placed in the hypopharynx. It is inserted blindly and usually does not require other accessory equipment for insertion. Often it is simply necessary to place the patient’s head in a sniffing position; the mouth opens by itself and thereafter inserts the device. Sometimes lifting of the lower mandible is required, and/or the index finger of the person who inserts the LMA is used to place it correctly4,13.

The size of the LMA is related to the patient’s weight: Size 3 is used in patients who are between 30 and 50kg, size 4 in patients between 50 and 70kg, and size 5 in patients between 70 and 100kg13. In one randomized controlled trial (RCT) that investigated LMA sizes, 5 vs. 4 in men and 4 vs. 3 in women, the incidence of POST in the PACU was higher in both groups that used the larger LMA. However, using a smaller sized LMA increased the risk of higher intra-cuff pressure14, which can be a risk for increased incidence of POST15, although this did not occur in this study. Another angle was addressed in a study using crossover design, which found that the larger LMA (4 in women and 5 in men) provided a better seal and significantly more optimal ventilation16. Therefore, it is difficult to generalize since many different variables need to be addressed in the choice of LMA size.
Incidence of Sore Throat and Hoarseness

The incidence of POST after endotracheal intubation varies between 44% and 64% of those patients surveyed\textsuperscript{17,18}. Several risk factors can lead to the development of POST after an ETT (Table 1), but the precise reason that the symptom emerges is still unclear. One plausible explanation might be an inflammatory process in the mucosa lining\textsuperscript{19}. The likely cause of the inflammation is thought to be ETT size as well as the cuff design and cuff pressure\textsuperscript{20}. In one study, the authors found that a high cuff pressure, \textit{i.e.} >30 cm. H\textsubscript{2}O, was the cause of tracheal lesions, and these correlated well to the development of a sore throat\textsuperscript{21}. Number of laryngoscopies has not been significantly associated with POST in several earlier studies\textsuperscript{17,22-24}.

The incidence of POST following an LMA is approximately 20%\textsuperscript{25}. It was once thought that POST from the use of an LMA is related partly to the insertion technique, \textit{i.e.} whether the cuff is inflated or deflated cuff. However, this does not seem to be related to the development of POST\textsuperscript{26-28}. When comparing a rotational technique (\textit{i.e.}, the cuff is inserted in the mouth and turned counter-clockwise until the hypopharynx was felt) \textit{vs}. a midline approach (\textit{i.e.}, the cuff is inserted in the patient’s mouth, holding the LMA as if it were a pen, and pressure is applied to the palate pharyngeal curve until hypopharynx is felt), the latter method seems to decrease the incidence of POST\textsuperscript{29}. Also, high cuff pressure, \textit{i.e.} >60 cm. H\textsubscript{2}O, was related to the development of sore throat\textsuperscript{30,31}. A possible confounding variable in all studies conducted on this issue is the fact that the LMAs used on the patients came from different manufacturers, \textit{i.e.} Pro Seal\textsuperscript{®}, Igel\textsuperscript{®}, LMA Supreme\textsuperscript{®}, and LMA Classic\textsuperscript{®}. A systematic review including three different brands of LMAs showed a decrease in POST after an LMA compared to an ETT\textsuperscript{25}. Inconsistent with these results was a study with the secondary aim of investigating differences in adverse upper airway symptoms (POST, PH, and dysphagia) caused by the Proseal\textsuperscript{®} LMA and the ETT. The study found no differences at two hours and 24 hours postoperatively in either symptom\textsuperscript{32}.

The incidence of PH is 30-49\% after an endotracheal intubation\textsuperscript{33-37}, and 7.5\% after laryngeal mask airway\textsuperscript{25}. The etiology of PH is different depending on whether it was caused by the ETT or the LMA. When the patient is intubated, there is a risk of vocal cord injury. In a study by Mencke \textit{et al.}\textsuperscript{37} the authors categorized the vocal cord sequelae by both location (uni-or bilateral) and type. In the authors’ categorization, types of sequelae included thickening of the vocal cords (localized swelling at the vocal process of the arytenoid cartilage), edema (swollen mucosa at the vocal cords), erythema (redness of the mucosa with surrounding inflammatory swelling), hematoma (caused by bleeding into the vocal cords), granuloma
of the vocal cords (granulation tissue remains as chronic, localized, rounded tissue), and arytenoid dislocation or luxation (displaced arytenoid with limited movement). In this study, the most common type of sequela in the patient was hematoma. The left vocal cord was more often affected than the right. Prolonged hoarseness can be caused by dislocation of the arytenoid cartilage.

PH associated with the LMA depends on the pressure in the cuff and results in neuropraxia of the laryngeal nerve, which in turn can cause unilateral vocal cord palsy.

**Inflammatory Pain**

Sore throat described in this thesis is most likely non-infectious, and refers to acute pain due to local tissue injury in the laryngeal area after general anesthesia with either an ETT or an LMA. Sore throat is an acute but transient phenomenon.

The pain can be categorized as superficial pain, and is different from deep visceral or deep somatic pain. A noxious stimulus to the mucosal membrane initiates a two-phased pain. Phase I is short-lived and mediated by A-delta fibers, followed by Phase II initiated by C-fibers. The pain continues until the healing process is completed. The main distinction between acute and chronic pain lies in the duration of pain: Chronic pain refers to pain that lasts longer than three months following the initial painful sensation.

When a mucous surface with sensory nerve innervation is damaged or injured, a complex series of events begins in the body. The cellular breakdown releases biochemical substances that directly stimulate receptors found in the free nerve endings. The impulse is conducted by different fibers, the fast A-delta myelinated fibers and the slower unmyelinated C-delta fibers. The A-delta fiber gives rise to strong and intense pain, while the C-delta fibers give rise to a diffuse and aching pain. All tissues are innervated by polymodal A-delta and C-delta receptors; there are also silent nociceptors, which are only activated by the inflammatory response. There are receptors that respond to only one kind of stimuli (e.g., heat) called heat nociceptors. There are also receptors that respond to several types of stimuli and they are called polymodal receptors. Tissue damage is always accompanied by an inflammatory process. Nociceptive pain is described as pain due to tissue damage and can be caused by mechanical stimulation of nociceptors. Different areas of the body have different densities of nociceptors. There are fewer pain receptors in the internal organs,
which makes it difficult for a patient to localize precisely pain emanating from the internal organs.

No study has yet pinpointed the precise location of postoperative sore throat and its precise etiology is still unclear. One hypothesis from a swine model is that POST is an inflammatory process involving the cytokine interleukin 6 (IL-6). This inflammatory process was confirmed in a small study in 14 patients undergoing short term intubation for a median duration of three hours. In this study, the levels of three cytokines, including IL-6, were measured from the tracheal lavage and were found to increase over time. The authors concluded that the human trachea might respond to a foreign subject, i.e. the ETT, by releasing inflammatory markers.

Pain perception is always personal and subjective. Pain is defined by the International Association for the Study of Pain (IASP) as

“an unpleasant sensory and emotional experience associated with actual or potential tissue damage.”

**Cuff Design and Cuff Pressure in the Endotracheal Tube**

There are two different types of cuffs, the low-volume high-pressure (LVHP) cuff and the high-volume low-pressure (HVLP) cuff. Both cuffs have advantages and disadvantages. The LVHP cuff has a small diameter and requires high intra-cuff pressure to overcome the low compliance in the cuff. There are two disadvantages of this high pressure: the risk of ischemia in the tracheal mucosa, and risk that the cuff might inflate in a noncircular fashion and injure the trachea. The HVLP is larger and correlates closely to the pressure in the trachea. Nonetheless, the LVHP cuff is associated with a lower incidence of POST than the HVLP cuff. The reason for this could be that the HVLP cuff has a larger diameter and a longer cuff length, and thus comes into more contact with the tracheal mucosa.

High cuff pressure exerts high pressure on the tracheal mucosa. The ideal cuff pressure has been suggested to be between 20-30 cm. H2O. A cuff pressure greater than 34 cm. H2O decreases the perfusion in the tracheal mucosa, and a total obstruction of blood flow occurs >50 cm. H2O. One risk of a low cuff pressure (i.e., seal pressure) is micro aspiration, especially with HVLP cuffs in patients admitted to the intensive care unit (ICU). This could be because excessive material in the cuff allows microparticles to pass through into the trachea, unlike when the red rubber LVHP cuff was used. Through these channels, fluid may pass to the lungs and result in micro-aspiration. The shape of the cuffs may also increase the risk of micro-aspiration.
Different techniques to fill the cuff have been described in the literature. What is known as the “predetermined technique” for inflating a cuff involves injecting a predetermined amount of air. An increase from 0.5 to 9.0 mL of air can increase the cuff pressure from 2 to 120 cm. H2O. It has been shown that there is an inter-individual variability in the volume of air needed in the cuff (2-4 mL. of air may be adequate for most patients to achieve a pressure between 20-30 cm. H2O), and an adequate seal.

The “minimal leak technique” involves the injection of a small amount of air into the cuff and thereafter the aspiration of a small amount of air until a minor leakage is noted at peak inspiration.

The “minimal occlusive volume technique” is almost the same as the “minimal leak technique”, the difference being that after inflation, a small amount of air is removed until a leakage is heard. The lowest possible volume of air is then injected again to attain a seal at peak inspiration. This technique is perceived to be better at preventing aspiration.

The final technique, and also the most unreliable, is palpation of the pilot balloon to assess the cuff pressure. This technique increases the risk of high cuff pressures.

Cuff pressure can change during surgery. One study reported that 86% patients had changes in cuff pressure when they were moved from the supine to the prone position in spine surgery with their head rotated to the right. Without continuously measuring cuff pressure, it is impossible to secure the airway and ensure that the patient is not harmed.

Predisposing Factors
Previous studies have highlighted different risk factors for POST and PH after an ETT. Some of these risk factors have been confirmed by multiple studies, while others have not. It is important to bear in mind when reading the studies that different brands and sizes of endotracheal tubes were often used. The patient scenarios are also different, and often the analysis is performed for men and women combined, which may add a gender bias. This makes it somewhat difficult to evaluate the external validity of the studies.
Table 1 Risk factors for POST in intubated patients described in earlier research

<table>
<thead>
<tr>
<th>Risk factors for POST</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs.):</td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td>Chen62</td>
</tr>
<tr>
<td>31-40</td>
<td>Hisham23</td>
</tr>
<tr>
<td>≤70</td>
<td>Honma63</td>
</tr>
<tr>
<td>Blood on the ETT</td>
<td>Biro64</td>
</tr>
<tr>
<td>High cuff pressure</td>
<td>Combes21, Ratnaraj65</td>
</tr>
<tr>
<td>Duration of surgery (minutes):</td>
<td></td>
</tr>
<tr>
<td>&gt;90</td>
<td>Kloub17</td>
</tr>
<tr>
<td>&gt;120</td>
<td>Chen62</td>
</tr>
<tr>
<td>ETT size</td>
<td>Hisham23, Stout11</td>
</tr>
<tr>
<td>Female sex</td>
<td>Biro64, Chen62, Christensen24, Higgins22, Maruyama66, Myles67, Ratnaraj65</td>
</tr>
<tr>
<td>Smoking habits</td>
<td>Biro64</td>
</tr>
<tr>
<td>Type of surgery:</td>
<td></td>
</tr>
<tr>
<td>ENT Surgery</td>
<td>Chen62, Christensen24, Hisham23,</td>
</tr>
<tr>
<td>Gynecology</td>
<td>Higgins22</td>
</tr>
<tr>
<td>Use of lidocaine spray</td>
<td>Maruyama66, Hara68</td>
</tr>
<tr>
<td>Use of naso-gastric tube</td>
<td>Honma63, Kloub17,</td>
</tr>
<tr>
<td>Use of oral airway</td>
<td>Kyokong69</td>
</tr>
</tbody>
</table>

POST=Postoperative Sore Throat  
ENT= Ear-Nose and Throat surgery  
ETT=Endotracheal tube
Table 2 Risk factors for PH in intubated patients described in earlier research

<table>
<thead>
<tr>
<th>Risk factors for PH</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>Yamanaka\textsuperscript{36}</td>
</tr>
<tr>
<td>ETT size</td>
<td>Stout\textsuperscript{11}, Al-Qahtani\textsuperscript{70}</td>
</tr>
<tr>
<td>ETT vs. LMA</td>
<td>Abdi\textsuperscript{71}</td>
</tr>
<tr>
<td>Female sex</td>
<td>Maruyama\textsuperscript{66}</td>
</tr>
<tr>
<td>No use of muscle relaxant</td>
<td>Mencke\textsuperscript{37}, Mencke\textsuperscript{72}</td>
</tr>
</tbody>
</table>

PH=Postoperative Hoarseness
ETT=Endotracheal tube size
LMA=Laryngeal Mask Airway

Methods of Assessment of Sore Throat and Hoarseness

The research on POST dates back to the late 1970’s\textsuperscript{73,74}. Different scales have been used to measure POST. Often it is poorly defined and described by the patient simply as a sore throat\textsuperscript{19}. The preferred scales to measure POST are a numeric rating scale (NRS), a visual analog scale (VAS), dichotomous answers or a four grade scale (with the numbers 0-3 corresponding to no, mild, moderate, and severe pain), presented here in a random order (Table 3) Since there is considerable variation in published studies on the incidence of POST due to the size of ETT used, the time-point for its measurement as well as the scales used to measure it, no consensus exists for the measurement of POST. When measuring PH, a binary scale is often used (yes/no) rather than more invasive but more precise methods such as a stroboscope\textsuperscript{36,37} or a voice recording\textsuperscript{35,75}. There is, however, a four-grade scale that has been used in a study by Mencke \textit{et al.}\textsuperscript{37}.

When should POST and PH be measured? Although there is no clearly defined time to do so, POST seems to be worst for the patient in the early postoperative period, and therefore it is important to measure it in the PACU\textsuperscript{76}. It is also important to ask direct questions in order to elicit clear responses from patients about POST\textsuperscript{77}. In contrast, PH can be a prolonged symptom that affects patients for varying amounts of time\textsuperscript{34,36,38}. Xu \textit{et al.} found that patients suffered from PH after an endotracheal intubation for lengths of time ranging from one day to 45 days, while one patient had PH for 155 days postoperatively\textsuperscript{38}.
Table 3 The influence of ETT size, gender and time of measurement on POST and PH

<table>
<thead>
<tr>
<th>Scale</th>
<th>Outcome variable</th>
<th>ETT size</th>
<th>Sex</th>
<th>Time of measurement</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS</td>
<td>POST</td>
<td>7.5♀</td>
<td>♂+♂</td>
<td>Between 12-24 h from extubation</td>
<td>Biro⁶⁴</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.0♂</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes/No</td>
<td>POST/PH</td>
<td>7.5♀</td>
<td>♂+♂</td>
<td>1h, 24h and after 1 week</td>
<td>Ratnaraj⁶⁵</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.5♂</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes/No</td>
<td>PH</td>
<td>6.0-6.5♀</td>
<td>♂+♂</td>
<td>Within 24 h</td>
<td>Al-Qahtani⁷⁰</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.0-7.5♂</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes/No</td>
<td>POST</td>
<td>7.5♀</td>
<td>♂+♂</td>
<td>Between 6-24h from extubation</td>
<td>Kloub¹⁷</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.5♂</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes/No</td>
<td>POST</td>
<td>?</td>
<td>♂+♂</td>
<td>24 h</td>
<td>Higgins²²</td>
</tr>
<tr>
<td>Yes/No</td>
<td>POST/PH</td>
<td>7.0♀</td>
<td>♂</td>
<td>In the PACU</td>
<td>Abdi⁷¹</td>
</tr>
<tr>
<td>NRS</td>
<td>POST/PH</td>
<td>7.5♀</td>
<td>♂+♂</td>
<td>2h and 24h</td>
<td>Combes²¹</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.0♂</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-3</td>
<td>POST</td>
<td>6.5♀</td>
<td>♂+♂</td>
<td>In the PACU</td>
<td>Chen⁶²</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.0♂</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-3</td>
<td>POST</td>
<td>7.0-9.0♀</td>
<td>♂+♂</td>
<td>?</td>
<td>Hisham²³</td>
</tr>
<tr>
<td>0-3</td>
<td>POST/PH</td>
<td>7.5♀</td>
<td>♂+♂</td>
<td>In the PACU and 24h</td>
<td>Kyokong⁶⁹</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.5♂</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-3</td>
<td>PH</td>
<td>7.5♀</td>
<td>♂+♂</td>
<td>24 and 72h</td>
<td>Mencke³⁷</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.5♂</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-3</td>
<td>POST/PH</td>
<td>7.0-8.0♀</td>
<td>♂+♂</td>
<td>In the OR and 24h</td>
<td>Maruyama⁷⁸</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.0-9.0♂</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-3</td>
<td>POST/PH</td>
<td>6.5♀ or 8.5♀</td>
<td>♂ and ♂</td>
<td>24-48h after anesthesia</td>
<td>Stout¹¹</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.0♂ or 9.0♂</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VAS=Visual analog scale. NRS=Numeric rating scale. POST=Postoperative Sore Throat. PH= Postoperative Hoarseness. PACU= Post Anesthesia Care Unit. OR=Operating room. h=Hours. ♂+♀= Analyzed as a single group. ♂ and ♀=Analyzed separately. ?=Not described
The Difference between Gender and Sex

Sex refers to the biological differences and chromosomal between men and a women\textsuperscript{79}. However, gender is more than the biological individual; it describes the femininity or the masculinity of a person\textsuperscript{80}. Gender involves the interaction of men and women and involves power and hierarchy\textsuperscript{79}. One concept is “doing gender” which can be described as a process which re-shapes in the actions that we perform as human beings\textsuperscript{79,81}. It can be difficult to contravene the norms of what society believes to be feminine or masculine behaviour\textsuperscript{79,81}.

Health care today often treats the male sex as a default; in short, what men do or say is the norm\textsuperscript{79,82}. Therefore, masculinity is seen as superior to femininity\textsuperscript{79}. Western medicine is strongly influenced by positivism and a search for the cause of a disease without necessarily incorporating culture, social factors, or subjectivity into research\textsuperscript{79}.

Research that investigates differences between men and women describes biological differences between the sexes largely without taking into account gender\textsuperscript{79}. Having said this, it is also important to acknowledge current research in medicine, which often takes gender into consideration, for example, differences between reported symptoms or behavior in men and women in contact with health care\textsuperscript{79,81}.

Pain and Sex/Gender

Responses to pain stimuli are thought to be taught during early childhood\textsuperscript{80}. Many studies have investigated sex differences in the responses to experimental stimuli, without any conclusive results. However, experimental studies have shown a difference between men and women in pain threshold and tolerance to pain\textsuperscript{80}. Whether these results are due to different expectations in gender-specific behaviour or differences in sex is still being debated.

There are several experimental studies in the literature concerning gender-specific expectations towards pain. One study investigated expectations of pain in men and women and demonstrated that both men and women expected the typical man to report less pain for common pain events\textsuperscript{83}. At the same time, results were presented from another study in which the observers of a short video clip rated men to have less pain than women. In other words, the female observers rated significantly higher pain intensity than the male observers and the women rated observed pain scores higher than the men\textsuperscript{84}.

However, in another study, another approach was used. Here 120 students were divided into three groups with equal numbers of men and
Sex Differences in Anesthesia
Greenspan et al. state, “We recommend that all pain researchers consider testing their hypothesis in both sexes, or if restricted by practical considerations, only in females.”

This is to reduce the risk of generalizing results that have been investigated only in males. More and more research points out that there are differences between men and women in the emergence from anesthesia, the quality of postoperative recovery, and pain response, as well as pharmacodynamic and pharmacokinetic response. It seems that women have a different recovery profile than men. Even though women emerge faster from general anesthesia, their Quality of Recovery (QoR) is poorer than that of men. Women rated higher pain scores in the PACU and in the first three days after surgery. Women also experienced more postoperative nausea and vomiting (PONV) and longer stay in the PACU than men. One explanation for the observed gender differences might be physical differences between the sexes. Men and women have differences in body mass index, percentage of body fat, and differences in total body water, and hormones.

Myles et al. suggest that there is a sex difference in the ability to report postoperative symptoms, and that women may find it easier to report symptoms to a nurse than men do. It is also possible that patients report...
Sore throat and hoarseness after general anesthesia symptoms differently to different healthcare workers. In one study, female patients consistently gave lower VAS pain scores to the RN than the surgeon91.

Satisfaction with Anesthesia

Satisfaction with anesthesia has been defined as,

“The balance between what is expected and the perception of what is received”92.

In a Delphi study, a panel of anesthesiologists’ investigated 33 common outcomes that may be important to avoid, from a patient perspective. The panel agreed that POST is a common postoperative outcome. However, when reporting how important POST would be from a patient perspective, the anesthesiologists placed POST just 25th out of the 33 outcomes93. When the patient perspective was investigated, the picture was somewhat different. Although POST was not the most important side effect to avoid even from a patient perspective, POST can decrease the experience of anesthesia itself18,94-96.

In order to improve patient satisfaction after anesthesia, studies have shown that it is important to provide proper preoperative information97,98, and a postoperative visit by the anesthesiologist or registered nurse anesthetist (RNA)92,99. It remains unclear how many postoperative visits are best for the patients, one99 or more than two92. Saal et al. reported that patients were dissatisfied with “continuity of anesthesia care” if they were not told who would conduct the postoperative visit. If the patient expected an anesthesiologist, they were dissatisfied if an RNA visited99. The majority of a cohort of ambulatory patients from Scotland was significantly more satisfied if they had someone to contact if a problem arose after discharge98. Also, patients are more likely to be highly satisfied when they are provided with clear and accurate information about the phases of anesthesia92. At 30 days after surgery, strong predictors of satisfied patients were clinical information, low postoperative pain scores in the PACU, and the final surgical outcome97.

What information the patient wants seems to differ between patient and professionals. One study from the Netherlands identified important areas of information observed from two perspectives, the surgeon’s and the patient’s. The results revealed that information about anesthesia e.g., type of anesthesia, variations in anesthesia, complications of anesthesia, sensations during anesthesia, and relief of tension, as well as information about the
early postoperative recovery were all highly significant from the patient’s perspective but not from the surgeon’s perspective\textsuperscript{100}.

The importance of decreasing minor adverse events was shown in a large study with over 10,000 patients. They were all interviewed within 24 hours after anesthesia for a number of events (i.e., POST, PONV, back pain, urinary retention, confusion, neurological deficit, myocardial infarct, hepatitis, renal failure and pain) and were asked to rate if they were satisfied or dissatisfied with the anesthesia care. The incidence of dissatisfied patients was 0.9\%, while 2.3\% were “somewhat dissatisfied”. When adjusted for patient and surgical factors, the results showed that any postoperative complications described earlier (pain and PONV excluded from analysis and analyzed separately) increased the risk of being dissatisfied (odds ratio (OR) 2.04, 95\% CI 1.64-2.56, p<0.001). Additionally the risk of patient dissatisfaction increased along with postoperative complications\textsuperscript{96}. This is supported by another large survey from Switzerland with over 12,000 patients who were interviewed between the second and fifth postoperative days. Patients rated POST and PH second and third, respectively, on the list of complications they found concerning. Their satisfaction level was generally high, but dissatisfaction was clearly associated with at least one adverse event\textsuperscript{3}. Also, women were at greater risk than men of dissatisfaction with pain management regimes\textsuperscript{101}. Therefore, it is important to investigate anesthesia quality with objective and valid instruments\textsuperscript{102}.
**RATIONALE**

Postoperative symptoms of sore throat and hoarseness after intubation can be annoying for patients. The exact cause of these symptoms is not fully understood. Selecting the size of the endotracheal tube in adults is often standardized and rarely customized. Previous studies have shown that women are more susceptible to sore throat after intubation, and the endotracheal tube size may be the cause of these symptoms. Only one study has previously examined the difference between the sizes of endotracheal tubes in a female population. It is therefore important to examine differences in the onset of symptoms in women if they were intubated with different sizes of endotracheal tube.

No observational study has previously examined a population of women intubated with endotracheal tube size 6.0. Therefore, examining a population of men and women in order to systematically understand and investigate intraoperative airway management and patient characteristics that lead to postoperative symptoms fills an important gap in our knowledge. Furthermore, establishing the differences between men and women in airway related symptoms is important so that endotracheal intubation can be performed safely and correctly.

Another factor that contributes to postoperative symptoms is the use of LMA, even though the incidence of POST is lower when using an LMA compared to an ETT. To my knowledge, there have been no studies that have evaluated the difference in pain localization, between ETT and LMA and none that have investigated differences between men and women on how they respond to ETT compared to LMA. Postoperative hoarseness following general anesthesia has also not been investigated thoroughly.

By filling these gaps in our knowledge, we may be able to reduce the risk of unnecessary suffering from POST and/or PH for patients undergoing general anesthesia.
AIMS

The overall aim of this thesis is to describe patients' postoperative sore throat and hoarseness after general anesthesia with endotracheal intubation or laryngeal mask airway. The thesis also aims to investigate the risk factors associated with post-operative sore throat and hoarseness, and to test methods that may prevent sore throat and hoarseness after a general anesthesia.

Specific aims:
I To compare whether women intubated with ETT size number 6.0 had less sore throat compared with women intubated with ETT size number 7.0. The secondary aims were to investigate the risk of hoarseness and discomfort from sore throat and hoarseness, as well as duration of these symptoms.

II To identify risk factors associated with POST and PH in women following endotracheal intubation. The aim was to add to our knowledge about predictors of sore throat and hoarseness in patients undergoing surgery with an ETT, in order to maintain a free airway.

III To describe independent factors that may be associated with the development of POST and PH after endotracheal intubation in adults, as well as whether there are any gender differences.

IV To determine the differences in the incidence of postoperative sore throat and hoarseness following laryngeal mask airway or endotracheal tube, and whether there are any specific gender differences in these adverse events, as well as to determine the location of sore throat and the duration of these symptoms.
ETHICAL CONSIDERATIONS

The Declaration of Helsinki and good clinical practice were followed in all four studies. Ethical approval was obtained from the Regional Ethics Committee, Uppsala, with the following reference numbers: 2008/023 (I, II), 2011/086 (III) and 2012/392 (IV).

Informed consent was obtained as follows: When eligible patients were referred to surgery, the department nurse sent an information sheet home to the patient. A form for informed consent was also included in the envelope. On the day of the surgery, before any premedication was administered, the researcher visited the patients and written consent was obtained. The aim and intentions of the study were carefully explained, as well as, the scales used and the reasons why patients’ reported outcomes were collected several times postoperatively (I).

In study III, the Regional Ethics Committee exempted written consent since no intervention was planned and only standard anesthesia care was used. Only verbal consent was obtained prior to anesthesia. The RNA asked the patient before induction if the patient consented to be questioned about POST or PH in the PACU. However, even non-written consent must be carefully documented and therefore the patient’s participation in the study was documented on the clinical research form (CRF) and in the anesthesia record. All patients were given written information about the aim of the study and the outcome measurement.

In study IV, eligible patients were recruited during the preoperative check-up visit or on visits to the Ambulatory Unit on the day of the surgery by the researcher or a trained research nurse. Written consent was collected before surgery. Consent to participation in the study was documented in the patient’s electronic data record and in the CRF.

In studies I, III and IV all patients were informed that they could withdraw at any time without affecting further anesthesia care. In order to protect patients’ privacy, the data collected were coded a manner such that no individual could be recognized.
METHODS

The studies included in this thesis are primarily quantitative in nature, including one study that has experimental design and three studies that are prospective but without experimental designs. Table 4 presents an overview of all four studies, which will be referred to as studies I-IV throughout the text.

Table 4 Study design of studies included in this thesis.

<table>
<thead>
<tr>
<th>Study</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Design</td>
<td>RCT</td>
<td>A prospective cross sectional study; a secondary analysis</td>
<td>A prospective observational study with a cross sectional design.</td>
<td>A prospective longitudinally study with a descriptive design</td>
</tr>
<tr>
<td>Participants</td>
<td>n=100 Women</td>
<td>n=97 Women</td>
<td>n=495 Men and women</td>
<td>n=301 Men and women</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outcome variables</td>
<td>POST: Four graded scale. PH: Binary scale. Discomfort: Four graded scale</td>
<td>POST: Binary scale. PH: Binary scale</td>
<td>POST: Four graded scale. PH: Four graded scale. Location: Five different measurements and a photograph</td>
<td></td>
</tr>
</tbody>
</table>

RCT=Randomized Controlled Trial. POST=Postoperative Sore Throat. PH=Postoperative Hoarseness. PACU=Post Anesthesia Care Unit.

Settings and Study Population

All studies were conducted in the Anesthesia Department at the University Hospital in Orebro. However, the patients were recruited from different surgical departments.

In studies I and II, the patients were anesthetized for the Plastic Surgery and Ear, Nose, and Throat (ENT) departments. Study III included patients from several surgical departments, including the Eye, Plastic, ENT, General Surgery, Orthopedics, Hand, Urology, and Gynecology departments. Finally, in study IV, the patients were recruited from the General Surgery-, Orthopedics-, Hand-, Urology, and Gynecology departments.
The patients were recruited between March 2008 and December 2008 (I-II), May, and September and November 2011 (III), and January and April 2013 (IV).

The inclusion criteria were as follows: women ≥18 years (I-II), men and women ≥18 years (III-IV), anesthesia for more than 90 minutes’ duration (I-II), elective surgery (I-IV), supine position (I-II), ASA I-II (I-II), oral intubation (I-IV) with one or two attempts at laryngoscopy (I-II), need for an laryngeal mask airway (IV), and clear understanding of the Swedish language (I-IV) and possessing of a telephone for a follow-up call (I).

Exclusion criteria were as follows: anesthesia with rapid sequence induction (I-II), the use of succinylcholine (I-II), surgery in the throat and mouth area (I-IV), an on-going throat infection (I-II, IV), acute surgery (III-IV), nasal intubation (I-IV), esophageal probe inserted, and expected duration of surgery >240 minutes (IV).

Of the 896 patients included in this thesis, 578 were women and 318 were men. Study I included 100 women. However, three was excluded (Figure 1), therefore 97 women are included in the analysis (I, II). In study III, 292 women and 203 men were enrolled. In study IV, 186 women and 115 men were enrolled. In one patient, several attempts were made to insert a Proseal LMA, but it was unsuccessful and he was subsequently intubated. Two men and one woman had to be intubated during surgery, because of in adequate ventilation using an LMA. These four patients were excluded from the analysis. Therefore, from a total of 889 patients enrolled, 574 were women and 315 were men.
Figure 1: Flow Chart of the participants in study I and II
RSI=Rapid Sequence Induction. ETT=Endotracheal intubation. PACU=Post Anesthesia Care Unit.

Abbreviation: RSI= Rapid sequence induction
Anesthesia

No attempt was made in any study to intervene with the departmental guidelines on the standard of care during anesthesia. Premedication was administered to patients who needed it in accordance with the anesthesiologist’s preference. General anesthesia could either include target-controlled anesthesia (TCI) with propofol and remifentanil, or inhalation anesthesia with sevorane or desflurane. In study I, nitrous oxide with oxygen was used during anesthesia. However, starting in 2011, more and more anesthesiologists began to prefer using oxygen in air, and by 2013 no nitrous oxide was used at all for the maintenance of anesthesia. Standard-monitoring including saturation, heart rate, non-invasive blood pressure, Bispectral index (BIS) mostly during TCI, end tidal carbon dioxide, and neuro muscular transmission intubated patients given muscle relaxant. The endotracheal tube used in all studies was Mallinckrodt Hi-Contour™ (Mallinckrodt, Athlone, Dublin, Ireland). The size for women varied from 6.0 to 7.0 and for men 6.0 to 8.0. The endotracheal cuff was filled with air and the intra-cuff pressure continuously measured in all studies. No lubricant was used on the endotracheal tube cuffs. The laryngeal mask airway (Unique, single-use, Shanghai, China and Proseal, non-disposable) used in study IV was size 3.0-4.0 in women and 4.0-5.0 in men. The appropriate size was left to the individual preference of the nurse or anesthesiologist. A water-soluble lubricant (Glidslem APL, Stockholm, Sweden) was used on the LMA cuff, and the cuff pressure was also measured continuously. In study I, no students were allowed to intubate but in studies III and IV, all personnel, regardless of intubation or LMA skills, were allowed to intubate or insert the LMA.
Outcome Measures
Postoperative sore throat and postoperative hoarseness were investigated in all studies. Other measurements included discomfort from symptoms and localizations of POST, as well as duration of symptoms.

Postoperative Sore Throat (Studies I-IV)
Determining the incidence of POST was the primary aim in studies I-IV. In all four studies, a four-grade scale was used with a cold as a point of reference:

0= No sore throat
1= Mild sore throat (less than with a cold)
2= Moderate sore throat (as with a cold)
3= Severe (more severe than with a cold)\textsuperscript{11}.

The degree of POST was evaluated several different times during the postoperative period (Table 5).

Postoperative Hoarseness (Studies I-IV)
PH was the secondary aim in study I, and a binary scale (yes/no) was used to assess whether it was present. A binary scale was also used in study II. PH was evaluated in studies III and IV using a four-grade scale:

0= No hoarseness
1= Mild hoarseness (perceived only by the patient)
2= Moderate hoarseness (noticeable during the interview)
3= Aphonia (complete silence/inability to speak)\textsuperscript{37}.

The degree of PH was evaluated several different times during the postoperative period (Table 5).

Discomfort (Studies I and IV)
To investigate if the emergence of airway symptoms uncomfortable for the patient, a four-grade scale was used:

0= No discomfort
1= Mild discomfort
2= Moderate discomfort
3= Severe discomfort

The degree of discomfort was evaluated several different times during the postoperative period (Table 5).
Localization of POST (Study IV)
In order to determine where the sore throat was localized in the throat, a photograph was developed by the researcher (MJ) (Figure 2). Initially, ten persons who had reported POST after anesthesia were contacted irrespective of whether they had had an ETT or an LMA. They were asked to locate POST, and requested to describe the symptom by using an adjective that they found easy to understand. They described the location in the throat, that had been sore (the pharynx, and above or below the larynx). None of the ten persons described pain in the mouth, a category that included the lips and tongue, but MJ added this category. One patient had POST for 14 days, high up in her chest, after an intubation. The researcher interpreted this likely to be in the carina, and therefore a fifth category was added (high up in the chest). The photograph was then shown to ten new patients in the PACU, and they all confirmed that it was easy to understand and use (face and content validity)\(^\text{104}\). The color photograph was then laminated.

Figure 2 Photograph for localization of the sore throat-frontal and lateral views of a woman. 1. In the mouth. 2. In the pharynx. 3. Above the larynx. 4. Below the larynx. 5. High up in the chest\(^\text{\textsuperscript{5}}\)
Figure 2 Photograph of localization of the sore throat— a lateral view of a man and in the mouth. 1. In the mouth. 2. In the pharynx. 3. Above the larynx. 4. Below the larynx. 5. High up in the chest.
Data-Collection

The personnel in the Anesthesia Department were involved in data-collection that was specifically recorded on the CRF as well as in the patients’ anesthesia record (I, III, IV) and also in the patients’ electronic data record in study IV. For studies I and IV, the researcher (MJ) and four colleagues collected the outcome measures in all time periods. In study III, approximately 15 assistant nurses/registered nurses (RN) in the PACU helped with data collection. Two studies have a cross-sectional design and reported a follow-up only in the PACU (II and III), while two studies (I and IV) had a longitudinal follow-up 96 hours postoperatively. In study IV, a follow-up call was made even after 96 hours to those patients who had not recovered (Table 5).

Table 5 Measurement recordings in study I-IV

<table>
<thead>
<tr>
<th>Study</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time of measurement</td>
<td>In the PACU, after 24 h. If symptoms at 24 h a follow-up call at 72 h and 96 h until symptoms resolved.</td>
<td>In the PACU</td>
<td>Ready for discharge from the PACU</td>
<td>Ready for discharge from the PACU, after 24 h. If symptomatic a visit or a follow up call at 48h, 72h and 96h until symptoms resolved.</td>
</tr>
</tbody>
</table>

PACU=Post Anesthesia Care Unit. h=Hours
STATISTICAL ANALYSIS

Descriptive and analytical statistics are used in all studies as appropriate (Table 6).

Table 6 Statistical analysis

<table>
<thead>
<tr>
<th>Analyses</th>
<th>Study I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Student’s t test for unpaired sample</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>z test for unpaired sample</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kaplan Meier</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Breslows test</td>
<td>X</td>
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<td></td>
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</tr>
<tr>
<td>Chi-square</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Fischer’s exact test</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Mann-Whitney U test</td>
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<td>X</td>
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<tr>
<td>Odds ratio</td>
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<td>X</td>
<td></td>
</tr>
<tr>
<td>Logistic regression</td>
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<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

Study I

The estimation of sample size was performed after literature review. The hypothesis was that change in ETT size from 7.0 to 6.0 would result in a 30 % reduction of POST in the PACU. Using a superiority approach with a power of 80 % and a p-value < 0.05 (two-sided), this suggested a total sample size of 85 patients. To cover for attrition, a total of 100 patients were recruited (n=50 in ETT 6.0 group, and n=50 in ETT 7.0 group). Descriptive data is presented as mean (SD) or number (%). Student’s t-test and the Mann-Whitney U test were used for statistical analysis. The Kaplan-Meier test and the Breslow test were also used as appropriate. Since all patients were evaluated preoperatively, a z-test for independent groups was considered appropriate. The z-test, which is almost the same as a chi-square test, was used to take into account the baseline measurement. These analysis were done manually, or using SPSS 15.0 for Windows software (SPSS Inc. Chicago, IL, USA).
Study II
In this study, a secondary analysis of data collected from study I was performed. A total of eight different independent variables were re-analyzed in order to predict potential risk factors for POST or PH in the early postoperative period. The variables analyzed included those identified previously (age, smoking, duration of anesthesia, and use of throat pack) as well as several new variables (Mallampati-classification, and Cormack & Lehane-classification). The variables were categorized into age (18-60/>60 years), smoking (i.e. smoker/non-smoker), Mallampati/Cormack & Lehan classification (I-II/II-IV), cuff pressure (≤20/≥20 cm. H 2 O), duration of anesthesia (≤193/≥193 min.), use of throat pack (yes/no), and ETT size (6.0 or 7.0). Bivariate analyses with Chi-square statistics, a 95% confidence interval (CI) and odds ratio (OR) were calculated. A logistic regression analysis was not performed, since results may be inconclusive with such a small sample. Statistical significance was set at p-value < 0.05. The statistical software SPSS 17.0 for Windows (SPSS Inc. Chicago, IL, USA) was used when performing all analyses.

Study III
This was an observational study, but a sample size was calculated in order to have at least 15 patients for each variable, which would require 450 patients. To cover for missing data, a total of 495 patients were included. Both univariate and bivariate analyses were used. A multivariate stepwise backwards conditional logistic regression model split by gender was also performed following bivariate analyses using Chi-square or Fischer’s exact test. Only the variables considered clinically significant were entered in this model. A new dummy variable was constructed for ETT size (normal ETT size for women 6.0 and for men, 8.0 vs. not normal ETT size for both sex, 7.0). The statistical software SPSS 17.0 for Windows (SPSS Inc. Chicago, IL, USA) was used when performing all analyses.

Study IV
Earlier research and a systematic review of the literature were used to estimate sample size. The literature is not consistent in reporting incidence of POST and potential differences between the sexes after an LMA. An earlier study reported similar incidence of POST after an ETT between men and women. Considering the published literature, the assumption was made that 35% of the patients would experience POST in the PACU after an ETT, compared to 21% of the patients with an LMA, and the power 80% and p-value < 0.05 (one-sided), the power estimation
suggested 127 patients per group would be needed. To cover for potential attrition, a total of 150 patients with an LMA and 150 patients with an ETT were included. For analytical reasons, the four graded scales used to measure POST, PH and discomfort were all dichotomized. The Chi-square-test was used to compare differences in POST/no POST, PH/no PH, discomfort/no discomfort between the groups. Mann-Whitney U test was used when analyzing group differences. Kaplan Meier analysis was also done to investigate the duration of the symptoms. The statistical software SPSS 17.0 for Windows (SPSS Inc. Chicago, IL, USA) was used when performing all analyses.

**Demographic, Background and Medical Variables (Studies I-IV)**

In all studies the following variables were collected: duration and type of surgery; pre-, peri-, and postoperative medication and use of other specific medications believed to affect POST/PH (muscle relaxant, anticholinergic and cortisone); ASA-, Cormack &Lehane-, Mallampati-classification; intubation attempts; person intubating the patient (RNA/MD) (I) and that person’s experience in intubation skills (III-IV); the patient’s age, height and weight (I-IV). BMI was calculated in study I. Other variables collected were smoking (I-II), dental plate (I-III), cuff pressure (I-IV), and throat pack (I-III). The two groups in study I was comparable with regard to demographic and background variables. There were no significant differences between the groups regarding opioid, cortisone, or anticholinergic consumption (I-II). In study IV, intubated patients had longer surgeries than patients with LMA, were more often inpatients, and stayed longer in the PACU.
RESULTS

This thesis has five main objectives, and the results will be reported accordingly. These objectives are:

- To describe the incidence and perceived discomfort of POST and PH.
- To explore the localization and the patient’s own description of POST.
- To evaluate the duration of symptoms.
- To determine risk factors for the development of airway symptoms.
- To investigate actions that reduces the symptoms.

Incidence of POST in the PACU (Studies I, III and IV)

The overall incidence of POST varies from 21-52% irrespective of ETT size in men and women (I, III-IV). The incidence of POST in women intubated with ETT size 6.0 was similar in studies I and IV. The incidence of POST in women intubated with ETT size 7.0 was also similar in studies I and III. The incidence of POST was 32-38% in men regardless of ETT size (III-IV). There were no significant differences in POST between men and women after an ETT (III-IV).

With an LMA, the incidence of POST was 19%, but there was significant difference between the sexes, with 26% of women and only 6% of men experiencing POST (p=0.003) (IV) (Table 7).
### Table 7 Incidence of POST in the PACU

<table>
<thead>
<tr>
<th></th>
<th>Study I</th>
<th>Study III</th>
<th>Study IV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Women</strong></td>
<td>n=97</td>
<td>n=292</td>
<td>n=185</td>
</tr>
<tr>
<td>ETT 6.0</td>
<td>10/48 (21)</td>
<td>94/263 (36)</td>
<td>24/88 (27)*</td>
</tr>
<tr>
<td>ETT 7.0</td>
<td>24/49 (49)</td>
<td>15/29 (52)</td>
<td></td>
</tr>
<tr>
<td>LMA 3-4</td>
<td></td>
<td></td>
<td>25/97 (26)</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td>n=203</td>
<td>n=112</td>
<td></td>
</tr>
<tr>
<td>ETT 6.0</td>
<td>0/1</td>
<td>23/61 (38)*</td>
<td></td>
</tr>
<tr>
<td>ETT 7.0</td>
<td>6/17 (35)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ETT 8.0</td>
<td>59/185 (32)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LMA 4-5</td>
<td></td>
<td>3/51 (6)</td>
<td></td>
</tr>
</tbody>
</table>

Presented as number (%). *Irrespective of ETT size

### Incidence of PH in the PACU (Studies I, III and IV)

The overall incidence of PH varied between 42-59% irrespective of ETT size in men and women (I, III-IV). There was no significant difference in PH between different ETT sizes in study I. However, the incidence of PH increased to 79% in women intubated with ETT size 7.0 in study III. In studies III and IV, the overall incidence of PH was similar, 59% in study III and 57% in study IV, regardless of ETT size. No gender differences were seen in either study.

However, the incidence of PH (33%) was lower if an LMA had been used. There were no differences in PH between the sexes after an LMA (IV) (Table 8).
Table 8 The incidence of PH in the PACU

<table>
<thead>
<tr>
<th></th>
<th>Study I</th>
<th>Study III</th>
<th>Study IV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Women (n)</strong></td>
<td>n=97</td>
<td>n=289</td>
<td>n=185</td>
</tr>
<tr>
<td>ETT 6.0</td>
<td>18/48 (38)</td>
<td>148/260 (57)</td>
<td>50/88 (57)*</td>
</tr>
<tr>
<td>ETT 7.0</td>
<td>24/49 (47)</td>
<td>23/29 (79)</td>
<td></td>
</tr>
<tr>
<td>LMA 3-4</td>
<td></td>
<td>32/97 (33)</td>
<td></td>
</tr>
<tr>
<td><strong>Men (n)</strong></td>
<td>n=203</td>
<td>n=112</td>
<td></td>
</tr>
<tr>
<td>ETT 6.0</td>
<td>1/1</td>
<td>35/61 (57)*</td>
<td></td>
</tr>
<tr>
<td>ETT 7.0</td>
<td>10/17 (59)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ETT 8.0</td>
<td>109/185 (59)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LMA 4-5</td>
<td>20/51 (33)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Presented as number (%) or otherwise noticed. *Irrespective of ETT size

**Discomfort from POST and PH (Studies I and IV)**

The discomfort from the symptoms was more severe when the women had been intubated with an ETT size 7.0 (p=0.02). Women intubated with ETT size 7.0 reported moderate to severe discomfort from sore throat more than those intubated with ETT size 6.0, who reported mild to moderate discomfort (I).

In study IV, more patients experienced discomfort from POST after an ETT than after an LMA (p=0.001) and PH (p=0.013) in the PACU. More patients still had discomfort 24 hours after an ETT than after an LMA (p=0.025). Similarly, PH was considered to cause discomfort by more patients, after an ETT than an LMA (p<0.001).

At 48, 72, and 96 hours, there were no statistical differences in perceived discomfort from POST and PH between patients who received ETTs and LMAs. There were no differences between men and women in reporting discomfort from POST and PH.
Description and Localization of POST (Study IV)

When the patients described the feeling in their throat in the PACU, the most common words used were: “dryness in the throat”, “feels like a cold”, “stinging pain”, “irritation or tenderness” and “a swollen feeling”. Some examples of descriptions of feeling in the throat of patients in the PACU are provided below.

Woman after an LMA who experienced severe POST, with moderate discomfort and mild PH with a mild discomfort:

“Dryness. Pain came suddenly when I woke up at the at the recovery room”

Man after an ETT who had moderate POST and PH with both symptoms causing a moderate discomfort from both symptoms:

“Dry. Feels like the beginning of a cold. Like a sore in the throat”

Descriptions from two other patients after 24 hours:

One woman who, after an ETT had mild POST and moderate PH, but moderate discomfort from both symptoms.

“Cough. Feels like dust in the throat. It is irritated. It feels like a mechanical injury. Cannot raise my voice”

Man after an LMA with no POST and moderate PH with mild discomfort.

“Cannot speak simply. The voice does not feel adequate”

Of the patients who reported pain in the PACU, this pain was localized to below the larynx after an ETT in 11 patients (24%), vs. 1(4%) after an LMA. In patients with sore throat above the larynx, the distribution of symptoms between ETT and LMA was as follows: in the pharynx n=10(22 %) vs. n=10(37%), above the larynx n=17(37%) vs. n=14(52%) and top of the chest n=1(2%) vs. n=1(4%), respectively. A few patients reported pain at two different sites. In the pharynx and above the larynx after an n=5(11%) in an ETT vs. 1(4%) in an LMA, and above and below the larynx was only present in n=2(4%) in an ETT, while no patients with an LMA reported this symptom (IV).

In study IV the patients who had POST in the PACU and at 24 hours reported that the pain was present during certain activities. Approximately 40% had POST during rest, speech, and swallowing regardless of whether an ETT or an LMA had been used (Table 9).
Table 9 Pain in the throat

<table>
<thead>
<tr>
<th></th>
<th>In the PACU</th>
<th>After 24 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LMA (n=24)</td>
<td>LMA (n=18*)</td>
</tr>
<tr>
<td>Pain during rest n(%)</td>
<td></td>
<td>1(5)</td>
</tr>
<tr>
<td>Men/Women (n)</td>
<td>0</td>
<td>0/1</td>
</tr>
<tr>
<td>Pain during speech n(%)</td>
<td>1(4)</td>
<td>0</td>
</tr>
<tr>
<td>Men/Women (n)</td>
<td>1/0</td>
<td>0</td>
</tr>
<tr>
<td>Pain during swallowing n(%)</td>
<td>12(50)</td>
<td>12(27)</td>
</tr>
<tr>
<td>Men/Women (n)</td>
<td>1/11</td>
<td>7/5</td>
</tr>
<tr>
<td>Pain at rest, during speech, and swallowing n(%)</td>
<td>9(38)</td>
<td>19(42)</td>
</tr>
<tr>
<td>Men/Women (n)</td>
<td>1/8</td>
<td>10/9</td>
</tr>
<tr>
<td>Pain during speech and swallowing n(%)</td>
<td>2(8)</td>
<td>8(18)</td>
</tr>
<tr>
<td>Men/Women (n)</td>
<td>0/2</td>
<td>4/4</td>
</tr>
<tr>
<td>Pain at rest and during speech n(%)</td>
<td>0</td>
<td>3(6)</td>
</tr>
<tr>
<td>Men/Women (n)</td>
<td>0</td>
<td>1/2</td>
</tr>
<tr>
<td>Pain at rest and during swallowing n(%)</td>
<td>0</td>
<td>2(4)</td>
</tr>
<tr>
<td>Men/Women (n)</td>
<td>0</td>
<td>1/1</td>
</tr>
</tbody>
</table>

*Two missing. ** One missing. LMA=Laryngeal Mask Airway. ETT=Endotracheal tube. PACU=Post Anesthesia Care Unit.

Duration of Symptoms (Studies I and IV)

Although the symptoms were predominant in the early postoperative period, they could remain over a longer period of time, with between 3% and 11% of women having symptoms after 96 hours (I and IV). There were no significant differences at any time during the follow-up after the PACU, irrespective of ETT size (Figure 3) (I). Study IV showed similar results at 24 hours, with 23% incidence of POST irrespective of ETT size or gender. After an LMA, the incidence of POST was 12% at 24 hours. The incidence of POST and PH when using an ETT vs. an LMA are shown in Figure 4 (IV). Although ETT size did not appear to affect the recovery from POST,
a Kaplan-Meier analysis with the Breslow test showed a trend towards faster recovery from POST after ETT size 6.0 (p=0.06) (I).

PH did not differ at any time during follow-up, regardless of ETT size. (I). The overall incidence of PH at 24 hours, 36%, was similar between studies I and IV. A patient with an ETT was free of symptoms after a mean of 4.6 days (95% CI 3.2-6.1), compared to 3.6 days (95% CI 3.0-4.3) after an LMA. Corresponding values for PH were 3.2 days (95% CI 2.3-4.2) after an ETT and 2.8 days (95% CI 2.4-3.3) after an LMA.

Four patients (3 after an ETT and 1 after an LMA) had postoperative symptoms they were all recovered after two weeks after anesthesia. All of them declined contact with the responsible anesthesiologist for further evaluation (IV).

Figure 3

![Figure 3](image)

* p= 0.006 ^

Postoperative incidence of sore throat, from mild to severe, in women intubated with ETT size number 6.0 compared with ETT size number 7.0.

Abbreviations: ETT=Endotracheal tube. PACU= Postanaesthesia care unit.

^Mann-Whitney U-test
Risk factors for POST and PH (Studies II and III)

Two studies (II, III) explored the risk factors for POST and PH after general anesthesia (Tables 10 and 11).

In women, the cut-off age for greatest risk of POST differed between the two studies. In study II it was >60 years, but in study III it was >40 years. ETT size 7.0 in women appeared to increase the risk of POST in the early postoperative period with an odds ratio of 2.8 (II). This was not confirmed in the multivariate analysis performed in study III, in which there was a non-significant trend toward a risk of developing POST in women. The larger ETT size in women also increased the risk for PH (III) (Table 10).

An association between high cuff pressure and POST was not found through bivariate analyses for men or women. However, when comparing changes within gender, there more women than men experienced POST when cuff pressure was between 21-30 cm. H$_2$O than when pressure was ≤20 cm. H$_2$O (p=0.043) (III).

On the other hand, low cuff pressure was associated with PH in women (II). Cuff pressure within normal range of 21-30 cm. H$_2$O seems to decrease the risk for PH in women (III) (Table 10). A contrast ratio was seen for the men included in study III, where normal cuff pressure (21-30 cm. H$_2$O) increased the risk for PH (Table 11).
Another risk factor for the emergence of POST in women was multiple laryngoscopies during intubation (III). This was, however, not confirmed for men (Table 10).

Men had an increased risk for POST when they had Cormack & Lehane classification Grade IV (p=0.009). Personnel with less experience (≤3 months) also increased the risk for POST in men, with an odds ratio of nearly 4 (Table 11).
Table 10 Risk factors for POST and PH in women

<table>
<thead>
<tr>
<th>At the PACU</th>
<th>Study II^</th>
<th>Study III^</th>
<th>Multivariate analysis in study III*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>P value</td>
<td>95 % CI</td>
<td>OR</td>
</tr>
<tr>
<td>POST</td>
<td>P value</td>
<td>95 % CI</td>
<td>OR</td>
</tr>
<tr>
<td>&gt;40 yrs</td>
<td>0.03</td>
<td>1.1-3.8</td>
<td>2.0</td>
</tr>
<tr>
<td>&gt;60 yrs</td>
<td>0.01</td>
<td>1.4-10.0</td>
<td>3.7</td>
</tr>
<tr>
<td>Throat pack</td>
<td>0.04</td>
<td>1.0-10.9</td>
<td>3.4</td>
</tr>
<tr>
<td>ETT size 7.0</td>
<td>0.02</td>
<td>1.2-6.5</td>
<td>2.8</td>
</tr>
<tr>
<td>Two or more laryngoscopies</td>
<td>0.006</td>
<td>1.3-5.6</td>
<td>2.7</td>
</tr>
<tr>
<td>PH</td>
<td>P value</td>
<td>95 % CI</td>
<td>OR</td>
</tr>
<tr>
<td>Cuff pressure ≤ 20 cm. H₂O</td>
<td>0.04</td>
<td>1.0-6.1</td>
<td>2.5</td>
</tr>
<tr>
<td>Cuff pressure 21-30 cm. H₂O</td>
<td>0.05</td>
<td>0.3-1.0</td>
<td>0.6</td>
</tr>
<tr>
<td>Cough during intubation</td>
<td>0.03</td>
<td>0.9-57.9</td>
<td>7.3*</td>
</tr>
<tr>
<td>Duration &gt; 240 min</td>
<td>0.01</td>
<td>1.4-26.5</td>
<td>5.9*</td>
</tr>
<tr>
<td>ETT size 7.0</td>
<td>0.02</td>
<td>1.1-7.3</td>
<td>2.9</td>
</tr>
<tr>
<td>Esophageal probe</td>
<td>0.02</td>
<td>1.2-10.8</td>
<td>3.6*</td>
</tr>
</tbody>
</table>

POST=Postoperative sore throat. PH=Postoperative hoarseness. ETT=Endotracheal tube. CI=Confidence Interval. OR=Odds Ratio. ^Analyzed with Chi-square. *Fischer’s exact test * Analyzed with stepwise backwards conditional logistic regression.
Table 11 Risk factors for POST and PH in men

<table>
<thead>
<tr>
<th>At the PACU Men</th>
<th>Study III^</th>
<th>Multivariate analysis in study III*</th>
</tr>
</thead>
<tbody>
<tr>
<td>POST</td>
<td></td>
<td></td>
</tr>
<tr>
<td>McIntosh blade 4</td>
<td>0.01</td>
<td>1.2-6.3 2.7</td>
</tr>
<tr>
<td>More than 3 month work experience for personnel</td>
<td>0.003</td>
<td>0.2-0.7 0.3</td>
</tr>
<tr>
<td>Less than 3 month work experience for personnel</td>
<td>0.001</td>
<td>1.7-8.3 3.8</td>
</tr>
<tr>
<td>More than one intubator</td>
<td>0.007</td>
<td>1.3-6.6 2.9</td>
</tr>
<tr>
<td>Perioperative naso gastric tube</td>
<td>0.04</td>
<td>1.0-4.1 2.1</td>
</tr>
<tr>
<td>Used stylet</td>
<td>0.01</td>
<td>1.2-6.0 2.7</td>
</tr>
<tr>
<td>PH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cuff pressure 21-30 cm. H2O</td>
<td>0.04</td>
<td>1.0-3.6 1.9</td>
</tr>
<tr>
<td>Cuff pressure ≤ 20 cm. H2O</td>
<td>0.04</td>
<td>0.3-0.9 0.5</td>
</tr>
</tbody>
</table>

POST=Postoperative Sore Throat. PH=Postoperative Hoarseness. ETT=Endotracheal tube. CI=Confidence Interval. OR=Odds Ratio
^Analyzed with Chi-square. * Analyzed with stepwise backwards conditional logistic regression
Decrease in POST and PH in a Clinical Setting (Studies I, III and IV)

Intubating women with ETT size 6.0 decreased the risk for both POST (p=0.002) (I) and PH (p=0.02) (III) in the PACU. However, using an LMA rather than an ETT in women did not appear to decrease the risk for POST (p=0.8), but the risk for PH decreased to 33% for both women and men compared to 57% after an ETT (p=0.001) (IV) (tables 6 and 7). Men, conversely, did benefit from an LMA, with a low POST incidence of 6% after an LMA compared to 38% after an ETT (p<0.001) (IV).

Women were more prone to suffer from POST than men if they had not received non-steroidal anti-inflammatory drugs (p=0.03). Finally, more women to men developed POST when succinylcholine was administered to assist intubation (p=0.05).
DISCUSSION

The main finding of this thesis is that POST and PH are common adverse events affecting almost half of all patients after general anesthesia. The symptoms are most common in the early postoperative period, but they can last several days postoperatively. Both men and women report discomfort from POST and/or PH, but risk factors contributing to the emergence of the symptoms differ by sex.

Postoperative Sore Throat
In this thesis, the incidence of POST in the PACU varied for women depending on ETT size; with a smaller ETT (size 6.0), 21-27% of patients experienced POST (I, II and IV) and with a larger ETT size (size 7.0), approximately 50% of patients experienced POST (I-III). The risk of POST thus increased almost threefold if an ETT size 7.0 was used, compared to smaller ETT (II-III). Biro et al. found similar incidence of POST, (44%), in women after an ETT size 7.5. Also, similar results were found with the study by Xu et al. who found an incidence of 23% using ETT size 6.0 and 42% when using ETT size 7.0 in women. Also, none of our patients required re-intubation from ETT size 6.0 to size 7.0 due to difficulties in ventilation (I, III, IV).

Study I showed efficacy when a smaller ETT size produced a lower incidence of POST. Furthermore, studies III and IV showed effectiveness when ETT size 6.0 is used in almost all women, and the incidence of POST continued to be lower than with ETT size 7.0.

An LMA is a good alternative to an ETT when there is no risk of regurgitation or aspiration, and therefore we were interested in comparing the incidence of POST in patients when an LMA was used. In line with earlier studies in which the authors reported a lower risk of POST, PH, and laryngospasm with an LMA, we also found in study IV a low incidence of POST, 19%.

The etiology of POST is not yet clearly understood. However, it has been shown that short term intubation releases markers of inflammation. Therefore, it is possible that injury to the mucosa following insertion of the ETT or the LMA starts an inflammatory process releasing inflammatory cytokines, which causes swelling in the mucosa. The swelling in the hypopharynx or larynx then affects the vocal cords, and the patient experiences POST and PH. This was confirmed in one study where the authors found a decrease in both POST and PH, after patients sucked on a Strepsils lozenge® five minutes prior to intubation. This lozenge is anti-inflammatory and prevents pain. In this study, the women were intubated with ETT
size 7.0-8.0 and men with size 7.5-8.5, which is, in my opinion, rather a large ETT. Lubrication of the distal end of the ETT with betamethasone gel had the same effect of decreasing both POST and PH\textsuperscript{112,113}.

Several other studies have been published on methods that aim to decrease POST, including: administering intravenous lidocaine\textsuperscript{114}, or filling the cuff with lidocaine solution\textsuperscript{115}, gargling with ketamine\textsuperscript{116}, or licorice\textsuperscript{117} five minutes prior to induction, or intravenous dexamethasone (Declan®)\textsuperscript{118}, and steroid inhalation (Flixotide Evohaler™) in the operating room\textsuperscript{119}.

The precise timing for evaluating airway morbidity postoperatively is still not known. We know that symptoms emerge during the early postoperative period, and, in many patients, disappear within 24 hours\textsuperscript{66}. Two studies suggests that POST peaks 6 hours postoperatively, after which symptom decreases\textsuperscript{76,109}. Increased incidence of POST in the PACU after either an ETT or an LMA is in line with previous studies (I-IV). Despite good postoperative pain management, many patients still experience discomfort of POST. Only a few patients in studies I and IV had long lasting symptoms, in some cases >96 hours.

No attempts were made to intervene as to the choice in anesthesia, volatile (sevorane) or total intravenous anesthesia in this thesis. Although the choice of anesthesia and the risk for POST/PH have not been analyzed, one study did suggest that type of anesthesia did not increase laryngopharyngeal complaints in patients\textsuperscript{120}.

**Postoperative Hoarseness**

One of our studies confirmed a significant reduction in PH in women when a smaller ETT size was used(III), a finding which is similar to some previous studies\textsuperscript{11,70}. The overall incidence of PH in the PACU, 57-59% (III-IV), after an ETT is, however, relatively high compared to some other studies reporting lower incidences\textsuperscript{34}. Our finding that 79% of women intubated with ETT size 7.0 reports PH in the PACU (III) has not been confirmed in the literature. Can this high incidence be the result of patient positioning during surgery, e.g. prone position? The relationship between positioning and ETT size was not significant in our study, possibly because of a small sample size (III). In one study, the authors investigated changes in cuff pressure caused by ETT displacement when positioning a patient from supine to prone during spine surgery. Postoperatively, at 24 hours after extubation, they found a low incidence of sore throat (17%) and hoarseness (11%)\textsuperscript{61}. A possible explanation for the low incidence in this study could be that the standardized questions were presented 24 hours postop-
eratively, when the incidence has usually reduced considerably. In study IV, we found a fairly high incidence of PH, 33%, after an LMA, which is somewhat surprising since the patients were not intubated. PH has been a known symptom even after an LMA, but the incidence was only 7.5% in a systematic review by Yu et al. study 25 that extracted data on PH from six studies. However, there was no information in this paper as to the time of evaluation. In our department, oxygen is administered routinely to all patients using a nasal prong in the PACU. Could PH be decreased if oxygen were not administered postoperatively to every patient, but only to those who need it? Preoperative fasting may also affect voice quality. One small study on 24 men, who were fasted during Ramadan showed a 50% increase in phonary effort and a significant decrease in voice pitch while fasting 121. As far as I know, the correlation between fasting and PH has not been investigated in a clinical setting. Perhaps this is also a plausible and contributing explanation for PH in the anesthetized patients. Another confounding factor for PH can be gastroesophageal reflux 122, a factor that was not studied in this thesis.

Hoarseness can be a problem for a long time ≥7 days, especially, if lesions or arytenoid dislocation have occurred during the intubation 36, 75. One strategy to alleviate hoarseness is to ensure good intubation conditions 37, 72. Another is to choose an appropriate ETT size 10, 11, 70. One method that might decrease the incidence of hoarseness after endotracheal intubation is a “non-touch extubation” which means that the patient is not stimulated in any way during awakening 123. To my knowledge, no study has investigated the extubation procedure and its correlation with POST or PH. Prolonged hoarseness, (≥ 6 days), did occur in three patients in study IV. One woman was hoarse for eight days after ETT size 6.0, one woman was hoarse for 14 days after ETT size 7.0, and one man was hoarse for six days after an LMA. Two of them expressed concern about their prolonged hoarseness. I therefore believe it is a symptom that needs to be followed up over a longer period of time. In a retrospective study of post-intubation phonary problems, the authors wished to raise awareness that patients suffering from postoperative hoarseness were sometimes not diagnosed with an intubation injury until several years after the procedure 124. They described the patients as frustrated, as they were often diagnosed with problems such as gastroesophageal reflux or allergy, when in fact their intubation injury was the underlying cause of their hoarseness 124.

Risk Factors for POST and PH
There is surprisingly little literature on risk factors for POST and PH. When risk factors are not known, subjecting all patients to a treatment
alternative that would benefit only few would be costly and probably un-scientific. Therefore, it is better to identify patients at risk for POST, and PH, and offer supportive therapy, either prophylactically or for management of the symptoms. When investigating different risk factors for the development of POST and PH, we found some new factors and others that have already been discussed in the literature.

Age has been reported earlier as a factor contributing to POST\textsuperscript{23,24,62,64}. The literature is conflicting as to which age groups are at risk for POST, (30-40 \textsuperscript{23,62}, > 60\textsuperscript{125}, ≤70\textsuperscript{63}), probably due to multiple factors that can contribute to POST. All of these studies analyzed men and women as a single group, and only one study reported an age group with an increased risk of POST in men(30-49 years)\textsuperscript{24}. The difference in age group risk we found in women in studies II (>60 years) and III (>40 years) is not easy to explain. Age group in men did not correlate with a higher risk of POST or PH in study III. It is possible that hormonal changes during menopause in women may increase the risk of POST, as the tracheal mucosa may be more sensitive, dry, and easily traumatized by the ETT. The correlation between the phase of menstrual cycle and POST has recently been investigated. However, this study only included women between the age 18-45 years and they found no significant association between menstrual phases and POST\textsuperscript{126}. The effect of menstrual cycles phase and its effect on overall postoperative recovery have, also, previously been investigated\textsuperscript{88}.

A throat pack in the hypo-pharynx was, unsurprisingly, a factor that contributed to POST. Although this was suspected to be a probable cause of POST in earlier studies\textsuperscript{17,127}, the association had not been confirmed. The correlation between Cormack & Lehane classification and POST was not confirmed in study II in women, but in study III, more men with Cormack & Lehane classification, Grade IV were found to experience POST in the PACU. This association had been analyzed before but not confirmed, which could be because the study analyzed both men and women as a single group\textsuperscript{111}.

One earlier study showed smoking to be a significant risk factor in development of POST\textsuperscript{64}. However, we did not find that smoking was a significant risk factor in study II, which could be due to the small number of smokers recruited in this study. The literature has shown conflicting results on whether duration of anesthesia is an independent risk factor for POST\textsuperscript{17,62,64}. In study II, we did not find any correlation between duration of anesthesia and POST or PH. However, in study III we found that more patients experienced PH after 240 minutes anesthesia. This was also the
finding of Yamanaka et al.\textsuperscript{36}, who found that long duration of anesthesia in patients having an ETT led to PH.

We found that low cuff pressure (≤ 20 cm. H\textsubscript{2}O) in women intubated with either ETT 6.0 or 7.0 was a risk factor for PH (II –III). This came as a surprise to us, and we found no support in the literature for such a relationship. This difference in results could be explained in several ways: Different ETT sizes may have been used\textsuperscript{128}, or the studies were not designed to study this factor\textsuperscript{129,130}. Also, a cuff that does not fit tightly to the tracheal mucosa may enable dry gas to pass through and cause PH. Lastly, the discrepancy could simply be due to the fact that cuff pressure has not previously been carefully analyzed as a risk factor\textsuperscript{60,116,117}. So, why does low cuff pressure increase the risk for PH? One possible explanation could be that low cuff pressure allows the ETT to move easily within the trachea during surgery, and this constant rubbing of the ETT against the vocal cords may cause PH. The presence of a cuff in the sub-glottic area could also affect the vocal cords. However, Minonishi et al. found that even when cuff pressure changed after supine to prone positioning of the patients and the ETT was displaced, there was a low incidence of POST or PH at the 24 h follows up\textsuperscript{61}. It has been suggested that the cuff should be placed in the correct position, approximately two cm. distal to the vocal cord\textsuperscript{4}. Thus, it is possible that the ETT may migrate during surgery or is not placed correctly during intubation, which may be one explanation why intubated men (with cuff pressure 21-30 cm. H\textsubscript{2}O) experienced an increase in PH (III). Another possible confounder is the fixation of the ETT. In 93\% of patients, the ETT was taped to the right cheek with no tape across to the left cheek (III). Poor fixation of the ETT may contribute to a high incidence of PH, as the ETT might be more easily displaced during surgery. To the best of my knowledge, there have been no studies performed with the aim of investigating the effect of different fixation techniques on the risk of POST or PH.

**Gender Differences**

No statistical differences were found between the sexes in POST and PH (III-IV). Previous studies have convincingly found that women are at greater risk for POST compared to men\textsuperscript{17,22,23,62,64-67}. However, these studies used ETT sizes 6.5\textsuperscript{62},7.0\textsuperscript{23,66} and 7.5\textsuperscript{64,65} while others do not state what ETT size was used\textsuperscript{22,67}. In contrast, the incidence of POST was only 19\% in patients who had an LMA with the rate even lower in men (IV). These findings are similar those of Rieger et al., except that the patients were interviewed about their symptoms in the evening\textsuperscript{107}. We found a similar incidence of POST after ETT or LMA in women (IV). Which airway device is best for female patients? Different perspectives need to be considered, as there is an
increased risk of oral trauma\textsuperscript{131} as well as depression of pulmonary functions following an ETT compared to an LMA in the early postoperative period\textsuperscript{132}. For instance, dental trauma after laryngoscopy was found in 39\% of patients who had been intubated, compared to 2\% who had an LMA, without any gender differences\textsuperscript{131}.

Sorensen \textit{et al.} found a 50\% incidence of PH, but they did not assess gender differences\textsuperscript{75}. Also a multiple logistic regression did not find gender as an explanatory variable to prolonged PH\textsuperscript{36}. A gender-researcher might imply that studies III-IV only present the differences between men and women on a biological level. It is, however, my belief, that all responses from patients involve their gender of the person not just their biological sex, and therefore their responses to the outcome in question involves the femininity/masculinity as well as the social gender of the individual. Awareness of these aspects of gender can help interpret the results. Furthermore, these results may contribute to minimizing gender bias, since many studies on POST and PH can be considered to be gender blind as they combine both sexes in analyzing their data\textsuperscript{22,27,62,64,66}. Few studies have split the data and analyzed men and women separately\textsuperscript{11}. Thus, study III and IV follow the recommendations to consistently analyze for sex differences and report the findings as suggested by Fillingham \textit{et al.}\textsuperscript{133}.

Some studies have found men to be reluctant to report adverse outcomes to personnel\textsuperscript{87}. This statement was confirmed in a study investigating gender role expectations. Young students were given a questionnaire, Gender Role Expectations of Pain (GREP). This demonstrated that both men and women thought the typical man reports pain less willingly than the typical woman\textsuperscript{134}. Also, in a survey that included 400 patients and investigated the patient’s fear and anxiety of anesthesia, the authors found that women were more anxious and troubled than men. Also patients experiencing anesthesia for the first time were more afraid of improper postoperative care, and more women than men were afraid of postoperative pain\textsuperscript{135}. Even so, there were no differences in reporting discomfort from POST and/or PH between men and women in study IV. The contradiction between the study just described and the result from study IV is not easy to explain. Could this be because of the studies were conducted in a relaxed environment free of gender role expectations, or because the questions were asked directly\textsuperscript{77}? Attitudes of both patients and personnel have been poorly investigated this area. However, the expectations and perceptions of patients and personnel might affect anesthesia care. Minor adverse events may also be perceived as inconsequential and therefore not addressed as important by patients or personnel. Also, personnel may think that such common
events as POST and PH are an “expected” and “normal” postoperative event, and therefore fail to take them seriously\textsuperscript{136}.

**Methodological Strengths and Limitations**
As in all studies, there are strengths and weaknesses in my thesis. The first study (I) was a randomized controlled study and therefore the risk of bias was minimized, while the other three studies (II–IV) were not. However, these represent real-life situations in a large population of patients, and this study construction has its advantages.

The patient population studied comes from the same study base, i.e., patients undergoing anesthesia in a single hospital in central Sweden. However, different surgical departments were included in the different studies. Drawing study participants from different departments has advantages, but may have caused some selection bias. Additionally, different patient groups with varying co-morbidities could have affected the result in different ways. For instance, the women in study I were from the Plastic- and ENT departments had slightly different risk factors compared to women from other surgical departments (III). It is, however, unlikely that there was something unique about the 896 patients included in all four studies. In studies III and IV, the patients were recruited consecutively by either the RNA (III) or the researcher and two research nurses (IV). A few eligible patients did not want to participate in study I, as they wanted to be assured that they would receive ETT size 6.0, fearing they would experience POST if they would receive ETT size 7.0. In study IV, however, time constraint for personnel was the primary limiting factor. Of the 301 patients included, only 10 declined participation. All of them had been waiting for a long time at the pre-anesthesia assessment clinic; they were hungry and tiered and just wanted to go home.

The decision to administer the questionnaire face to face (I, III and IV) was made in order to minimize attrition. This is also why personal contact was made during the follow-up call or visit in the patients ward (I, IV)\textsuperscript{137}. There were few patients lost who received follow-up by telephone calls, one in study I, and four in study IV. Therefore, I believe that direct patient contact in the postoperative period ensures a high patient response on subsequent follow-up interviews and should be normative.

The strength of study I is its design, a randomized controlled trial (RCT), which controls the internal validity in a strong way\textsuperscript{138}. The drawback with of an RCT is the fact that it can be perceived as experimental due to the inclusion and exclusion criteria’s and does not replicate a real-life situation. The results, therefore, represent how an intervention may affect efficacy and do not necessarily reflect how well the intervention
would affect the patients when different confounders in the intraoperative care are allowed to react with the experimental variable. If I were redesigning the study today, I would have included men in study I and investigated whether different ETT sizes in men increase or decrease POST and PH.

Study II was a hypothesis generating study in which I wanted to explore risk factors in women intubated with ETT size 6.0. When re-analyzing data incorporating new variables, new correlations can be analyzed and new research questions can be posed. For instance, the secondary analysis of our data from study I revealed new, previously unreported relationships between PH and cuff pressure. However, this result needs to be interpreted with caution since the sample size is small and the result cannot be generalized to the male population.

When analyzing relationships between variables it is important to bear three questions in mind. First, does the cause come before the effect, *i.e.*, was the ETT placed before POST and PH developed? Second, is if the relationship plausible? And third, has the relationship been reported in earlier research? If the answer to all three questions is yes, it is more likely that a true relationship has been found. Even if a study has a small sample size, it can add to the literature in exploring and describing associations.

Study III, with its cross-sectional design, has several strengths as well as limitations. This study included a heterogenic group of men and women from different surgical departments. This heterogeneity improves the external validity, but there could be a selection bias since the groups are not comparable due to several confounders not controlled for in this kind of study design. However, a cross-sectional design may be preferable when describing a certain phenomenon at a specific time, in this study POST and PH in the PACU. This observational study is unique in that we studied women intubated with ETT size 6.0 and analyzed men and women separately. To the best of my knowledge this has not been done before. One limitation in this study was that the RNA had to receive verbal consent from the patient before induction of anesthesia, and due to memory lapses and a stressful work environment, this was forgotten in a number of eligible cases. How many eligible patients who were inadvertently not recruited into the study are unknown? The self-made clinical research form (CRF) was considered easy to fill out by personnel, but the third part concerning extubation, was sometimes missed when the patients were transferred to the PACU. Another limitation in the study design can be that some may see it as a “fishing expedition”, searching for relationships with several different variables. However, we did confirm some of the risk factors present-
ed in study II and also found interesting new variables to inspire future research. There is, however, always a risk of spurious associations, and therefore new research with randomized controlled designs is necessary to investigate these relationships further.

One possible limitation of study IV is the study design. Randomization of the independent variable, ETT or LMA, was not possible since certain operations require muscle relaxants and therefore an LMA is not always suitable. Therefore, the groups are not quite comparable, with more inpatients and longer surgeries in the ETT group. The sample size was not calculated by sex. Therefore the study may have a gender bias, and it may be underpowered and unable to detect small differences between the groups. The results must consequently be interpreted with caution. This study reflects a real-life situation with no attempts to influence insertion of the LMA or to control the experience of the personnel in any way. During data collection, many patients spontaneously pointed both at the photograph and at their own throat in order to clarify the precise location of the sore throat. Although my intention was to get the patient’s own description of how the pain in their throat, was perceived, this was not as successful as I had hoped. The patients were tired in the PACU due to residual effects of anesthesia, but many of them also had difficulty in verbalizing, the precise feelings in their throat. Perhaps it would have been better to offer them standardized words to choose from such as “itching”, “aching”, “swollen”, etc. Another approach would have been to use a quality-of-recovery scoring system140.

Another possible criticism is that several persons intubated the patients in all three studies, which could affect the studies’ reliability. Although this is true, in study I no students were allowed to intubate, while in studies III and IV, all personnel were allowed to intubate. The latter condition enhances the external validity of the studies and replicates a real-life situation in many anesthesia departments.

In all studies in this thesis, the same POST scale was used. I believe that the POST scale is sensitive enough to determine those who had a sore throat, and I doubt a second flexible fiber-optic evaluation of the mucosa would have improved the validity. The patients’ self-reporting of a sore throat may be subjective, but reflects their own personal experience, which is as important as an objective verification using fiber-optic examination. In one study, the authors performed fiber-optic bronchoscopy in patients who had been intubated, and found that a local patchy congestion or a formation of patchy hemorrhagic ulcerations, were associated with complaints of POST60. These results validate the fact that a patient experiences POST when the mucosa is injured. The advantage of the POST scale we
used was that the point of reference, a common cold, was easy to understand. In study IV many patients confirmed that the feeling in their throat was “just like a cold”. However, this scale has not been as evaluated, as the VAS scale has for postoperative pain\textsuperscript{141}. There is no consensus in the literature on what constitutes POST some authors even define a sore throat as pain including hoarseness \textsuperscript{17,22,142} and there may thus be a risk of presenting results between studies that are not comparable. To improve the scale used in this thesis, the outcome in question, PH, measured using a four-grade scale after study I. This scale is still subjective, but this time also included a level at which the hoarseness was noticeable for the interviewer (grade II). This was one way to further introduce objective criteria into measuring PH without performing invasive procedures in evaluation of the vocal cords\textsuperscript{37}. Another possible method of evaluation could be voice recording\textsuperscript{75} which would have validated PH even further. That said, Jones \textit{et al.} found a highly significant positive correlation between patients’ subjective assessment of PH and the evaluation of a speech therapist using a voice recording device\textsuperscript{143}. One advantage of using non-invasive methods for evaluation is increased patient participation and minimal dropout. The patients were keen to participate in the studies so that they could help improve care for future patients, particularly because the tests were performed were completely non-invasive, easy to understand, and not harmful in any way, a fact that patients confirmed in the follow-up telephone call in studies I and IV.

The strength of my studies is their broad selection of patients of different ages and both sexes who underwent operations in different surgical specialties. This diversity means that the results can be generalized to some extent. There is, however, a risk for pre-existing differences between two groups that should be considered\textsuperscript{144,145}.

There is always a risk of reporting bias in a study design in which information is collected from patients\textsuperscript{144}. Specifically, patients sometimes report different pain scores, depending on who is asking the question; in one study, patients reported higher pain scores to the doctor than to the nurse\textsuperscript{91}. This was not an issue in my studies since a nurse asked the relevant questions to all patients. In order to minimize the risk of recall bias, all questions to patients were formulated in the following way” Do you have ...... now?”\textsuperscript{144}. Similarly, during the follow-up, we evaluated how patients felt at the time and did not evaluate the outcome measure retrospectively (e.g., "How intense has the pain in........been in the last 24 hours?")). The latter question would require some degree of recall, which can lead to biased results.
Another limitation is that in study I extubation was not standardized or recorded. However, in study III, late or early extubation was recorded. These variables were not found to have a significant association with POST or PH.

Another drawback of all studies may be the interpretation of the results in relation to gender. Men and women are variables in an analysis and there is a risk for over-interpretation of results between the groups, since the results obtained may be due to differences between individuals, and not because of the sex of the person. However, I believe it is important to understand possible differences between men and women that may be evident from these studies in order to plan treatment correctly.

Clinical Implications and Future Studies
This thesis has highlighted postoperative symptoms that affect our patients on a daily basis. In order to provide good anesthetic care to patients, it is important that the doctor or nurse provide correct preoperative information. The type and amount of information provided may depend on the patient’s need for information as well as the knowledge and awareness of the individual who provides the information. All patients not aware of all aspects of anesthesia, and sometimes the caregiver may consider POST and PH of minor importance compared to other perioperative adverse events. Although this may be true, the individual patient who wakes up after an anesthesia with no other adverse events except a severe sore throat or hoarseness is still not satisfied with the anesthetic. This was confirmed during my studies, since several patients expressed surprise that they had woken up with a sore throat. Knowing that this is a common adverse event following anesthesia eased their experience of having POST and/or PH.

I believe it is important to regularly exercise quality control postoperatively in an effort to improve the quality of anesthetic care in the postoperative period, as well as to monitor any airway problems and the quality of recovery for our patients.

Providing information to patients is a complex problem, and sometimes the information received can be difficult to process for the patient. Therefore, in order to improve quality of recovery, written information regarding anesthesia care should be given to all patients prior to surgery. Furthermore, the patients should also be encouraged to contact the anesthesia services pre-and postoperatively, in order to discuss concerns about anesthesia as well as the common adverse events following anesthesia.

The Helsinki Declaration on Patient Safety in Anesthesiology states that:
“Patients have an important role to play in their safe care which they should be educated about and given opportunities to provide feedback to further improve the process for others”146,147. Thus, it is also important to have knowledge about minor adverse events in order to be able to improve anesthesia care. The importance of proper documentation regarding intraoperative airway management is also an area that could be improved. In order to help postoperative nurses in their care of patients, documentation of perioperative events is important. These could include whether there were multiple attempts at intubation or inserting the LMA, or if blood was seen on the ETT cuff during extubation or on the LMA cuff during its removal.

A number of patients in study IV who had problems with POST and informed the personnel did not receive anything to relieve the pain they reported, or they were not helped at all by the treatment offered. Some patients reported difficulty in sleeping during the first night after surgery because of the throat pain. This is a sign of that personnel did not have sufficient knowledge of how to reduce the symptoms; it also reflects an expectation that this is a “normal” phenomenon following anesthesia. Assessing patient satisfaction with anesthesia postoperatively, it can help us improve the care of our patients in the future.

Since ETT size 6.0 is almost always used in women today, in our department, following our first study the incidence of POST has decreased considerably. However, no such intervention has been made for men, and the ETT size in men is something that needs to be discussed further. The reduction in tube size did not seem to solve the problem of postoperative hoarseness which was still present in more than 50% in patients in studies III and IV.

A number of questions for further research have arisen in my mind as I have conducted my research. Some of these include:

- How much or how little pre- and postoperative information should be given to the patients? Does providing written information help avoid overwhelming patients with information?

- Can patient satisfaction be improved through systematic data collection regarding recovery period, focusing on the four P’s (PONV, PAIN, POST and PH)?
• Can a smaller-sized ETT in men decrease POST and PH?

• Can a different method for fixation of the ETT help in decreasing POST and PH in the early postoperative period?

• Are there interventions that can decrease PH such as postoperative oxygen?

• What is the role of cuff pressures in the development in PH in men and women?

• Is it possible to individualize the cuff pressure, but also balance the risk for regurgitation, aspiration and without increasing the risk for development of PH?

• Could an LMA designed for women help decrease of POST and PH?
CONCLUSIONS

- Endotracheal tube size 6.0 decreased postoperative sore throat in women in the early postoperative period (I).

- Endotracheal tube size 7.0 increased the risk for postoperative hoarseness in women in the early postoperative period (III).

- The airway symptoms were a discomfort for both men and women (I and IV).

- Sore throat can be located by the patients, who can therefore guide personnel to provide the proper relief off these symptoms (IV).

- Risk factors involved in the emergence of symptoms of POST and PH vary between men and women (II and III).

- A low cuff pressure in women increased the risk of hoarseness (II and III).

- Use of laryngeal mask airway compared to endotracheal intubation decreased the incidence of sore throats in men (IV).

- In women there was no difference in sore throat regardless of whether an LMA or an ETT was used (IV).

- No gender differences in hoarseness were found (III and IV).

- Hoarseness lasted about three days regardless whether an LMA or an ETT been used (IV).

- Sore throat lasted approximately five days after an ETT and four days after an LMA (IV).
SUMMARY IN SWEDISH

Ont i halsen och heshet postoperativt efter en generell anestesi med antingen en larynxmask (LMA) eller en endotrakeal tub (ETT), ett vård relaterat lidande som är vanligt förekommande bland våra patienter. Den totala incidensen för ont i halsen efter en endotrakeal intubation varierar mellan vilken population och intraoperativ miljö som studerats, den kan variera mellan 44-67 %.

Risken för ont i halsen hos kvinnor har varit nästan dubbelt så hög jämfört med män i tidigare studier. En trolig orsak till resultatet kan vara endotrakealtubens storlek. Incidensen hos kvinnor kan variera mellan 40-68 %. Incidensen hos män varierar mellan 9–40 %. Postoperativ heshet efter en ETT har en incidens på 40-50 % och 7.5 % efter en LMA.


Det övergripande syftet i aktuell avhandling är att beskriva patienters postoperativa smärta och heshet i halsen efter en generell anestesi, att undersöka vilka riskfaktorer som associerar till postoperativ smärta i halsen och till heshet, samt att testa åtgärder som kan lindra ont i halsen och heshet efter en endotrakeal intubation.

Delarbete 1

Det primära syftet med studien var att jämföra om kvinnor intuberade med endotrakeal tub nummer 6.0 hade mindre ont i halsen än kvinnor intuberade med endotrakeal tub nummer 7.0. Sekundära syften var att undersöka skillnader i heshet mellan grupperna och hur besvärliga symptomen av ont i halsen och heshet upplevdes, samt durationen av symtomen.

En kontrollerad randomiserad studie där 100 kvinnor inkluderades konsekutivt från elektiv kirurgi på plastikkirurgisk och öron- näsa - hals avdelningen (Örebro Universitetssjukhuset). Kvinnorna randomiserades till en av två grupper via en randomiseringslista skapad av en statistiker: ETT nummer 6.0 innerdiameter (ID) (n= 50) eller ETT nummer 7.0 ID (n=50).
Utvärdering av ont i halsen och heshet skedde baseline (före nedsövning), på postoperativ avdelning och efter 24 timmar. De som hade symtom vid 24 timmars mätning följdes upp efter 72 och 96 timmar fram tills att de var fria från symtom.

Resultatet visade att det var det en statistisk signifikant skillnad mellan grupperna, där fler kvinnor som varit intuberade med ETT 7.0 hade ont i halsen och mera besvär av ont i halsen jämfört med de kvinnor som varit intuberade med ETT 6.0 på uppvakningsavdelningen. Därefter fanns inga signifikanta skillnader mellan grupperna därefter. Det fanns inga signifikanta skillnader i heshet mellan grupperna vid något mättillfälle. Duration av ont i halsen och/eller heshet var 16,5 % hade fortfarande symtom efter 72 timmar och 11 % hade kvarvarande symtom efter 96 timmar.

**Delarbete 2**

Syftet var att undersöka vilka riskfaktorer som associeras med ont i halsen och heshet hos kvinnor i samband med en endotrakeal intubation.

En sekundär analys med kvantitativ metod, med tvärsnittsdesign av insamlad data från delarbete 1. Data från 97 kvinnor inkluderades och åtta olika variabler analyserades som potentiella riskfaktorer till ont i halsen och heshet.

Resultatet visade att för kvinnor med en ålder över 60 år, om en svalgpackning använts peroperativt samt om ETT 7.0 använts ökade risken för ont i halsen postoperativt. För heshet visade endast en variabel signifikans och det var ett lägre kufftryck (≤ 20 cm. H₂O) ökade risken för postoperativ heshet.

**Delarbete 3**

Syftet var att beskriva samband mellan intraoperativ luftvägshantering och kön i uppkomst av ont i halsen och heshet postoperativt.

En kvantitativ prospektiv observationsstudie med tvärsnittsdesign. Totalt inkluderades 495 patienter, varav 292 var kvinnor och 203 var män från åtta olika kliniker. Ett flertal variabler analyserades mot ont i halsen och heshet.

Resultatet visade att det inte var någon skillnad i ont i halsen eller heshet mellan män och kvinnor. Resultatet påvisade att män och kvinnor hade olika riskfaktorer för uppkomst av ont i halsen och heshet. Enligt den logistiska regressionen ökade risken för ont i halsen hos kvinnor om de la-ryngoskoperas ≥ 2 gånger i samband med intubationen och om ETT 7.0 använts peroperativt. Risken för heshet ökade om ETT 7.0 använts, om kvinnan hade haft en esofagal temperatur prob peroperativt samt om
kufftrycket varit ≤ 20 cm. H₂O. Männen hade mer ont i halsen om de intu-berats av personal med kort erfarenhet inom anestesi ( ≤ 3 månader). Ris-ken för heshet minskade om de hade ett lågt kufftryck ≤ 20 cm. H₂O.

Delarbete 4
Det primära syftet var att utvärdera postoperativa skillnader i ont i halsen och heshet mellan larynxmask och endotrakeal tub samt om det fanns några könsskillnader. Vidare att studera smärtans lokalisation i halsen och duration av symtom.
Resultatet på den postoperativa avdelningen visade att det var ingen signifikant skillnad i ont i halsen och heshet mellan män och kvinnor, oberoende av om de varit intuberade eller haft en LMA. Fler patienter hade ont i halsen och var hesa och uppgav att det var besvärande eftersom en ETT än efter en LMA. För kvinnor var det ingen signifikant skillnad i ont i halsen oavsett om de haft en LMA eller en ETT. Däremot hade färre män ont i halsen efter en LMA än efter en ETT. Fler patienter beskrev lokalisationen av smärtan i halsen att vara i svalget efter en LMA och en ETT. Flere patienter hade ont ovanför larynx och nedanför larynx. Smärtan i halsen var nävarande både i vila, vid tal och vid sväljning hos 38 % av de som haft en LMA och 42 % hos de som varit intuberade. Du-rationen av symtom skiljde sig inte mellan LMA och ETT, i genomsnitt hade patienterna ont i halsen i 4,6 dagar efter en ETT och 3,6 dagar med en LMA. Heshet kvarstod i 3,2 dagar efter en ETT och 2,8 dagar efter en LMA.
Sammanfattningsvis visade denna avhandling att ont i halsen och heshet efter en generell anestesi drabbade många patienter. Symtomen kunde finnas kvar i flera dagar efter anestesi. Färre kvinnor fick ont i halsen och blev hesa om ETT 6.0 användes istället för ETT 7.0. Fler kvinnor än män fick ont i halsen efter en LMA. Riskfaktorerna som bidrog till uppkomst av ont i halsen och heshet varierade mellan kvinnor och män. Resultaten från avhandlingen är kunskap som kan ligga till grund för delar i personcentre-rad anestesiologisk omvårdnad och i individanpassad pre- och postoperativ information.
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