Gynecologic Oncology 139 (2015) 559–567

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Review Article

The sentinel node procedure in early stage cervical cancer, taking the next step; a diagnostic review

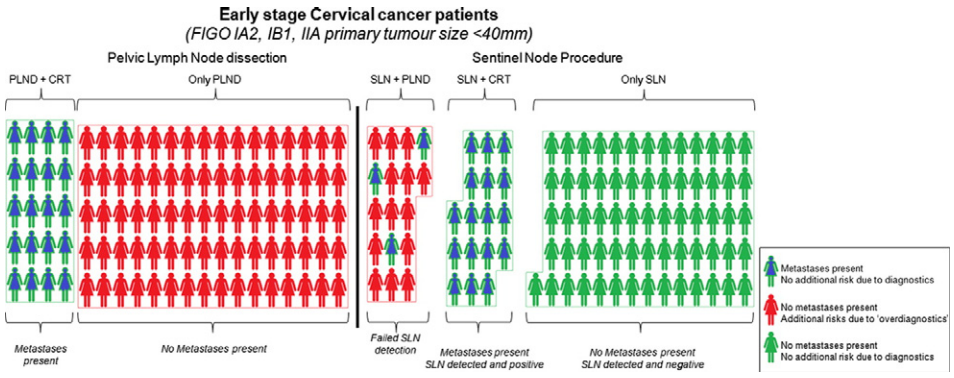
Casper Tax [a,*], Maroeska M. Rovers [a,b], Corine de Graaf [c], Petra L.M. Zusterzeel [c], Ruud L.M. Bekkers [c]

[a] Radboud University Medical Centre, Radboudumc Institute for Health Sciences, Department of Operating Rooms, P.O. Box 9101, 6500 HB Nijmegen, the Netherlands
[b] Radboud University Medical Centre, Radboudumc Institute for Health Sciences, Department of Health Evidence, P.O. Box 9101, 6500 HB Nijmegen, the Netherlands
[c] Radboud University Medical Centre, Radboudumc Institute for Health Sciences, Department of Gynaecology, P.O. Box 9101, 6500 HB Nijmegen, the Netherlands

HIGHLIGHTS

- We identified a subgroup in whom a SLN may replace a PLND.
- Ultra staging alone led to a sensitivity of 94%, NPV ranged from 91 to 100%.
- Additional prerequisites led to a sensitivity of 99%, NPV ranged from 97 to 100%.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 20 August 2015
Received in revised form 23 September 2015
Accepted 24 September 2015
Available online 28 September 2015

Keywords:
Sentinel node
Cervical cancer
Diagnostic accuracy
Systematic review
Diagnostic review

ABSTRACT

Objective. Recent reviews on the sentinel lymph node (SLN) procedure in cervical cancer have shown that bilateral SLN detection and ultra staging are safe and superior options compared to a unilateral detection, frozen section and H&E analysis. So far, nobody identified a subgroup of patients in whom a SLN procedure may replace pelvic lymph node dissection (PLND).

Methods. We searched PubMed, Embase, CINAHL and Cochrane from inception up to November 26, 2014. Studies reporting SLN detection, and/or histological outcome of the SLN were included. Methodological quality was assessed with the Quality Assessment of Diagnostic Accuracy Studies tool by two independent reviewers. Data to complete 2 × 2 contingency tables were obtained, and patient-, study- and technique characteristics were extracted. Results were pooled and plotted in forest plots.

Results. Forty-seven studies (4130 patients) were analyzed. Pooled data of diagnostic accuracy on ultra staging (18 studies; 1275 patients) showed a sensitivity of 94% (95% CI 80–99%) and negative predictive values ranging between 91 and 100%. After ultra staging, 19 false negative results remained. Prerequisites such as early FIGO stage (IA2, IB1, IIA primary tumor size <40 mm), no suspicious pre-, and per-operative lymph nodes, and bilateral negative SLNs after ultra staging resulted in 1 remaining false negative result among 1257 patients (0.08%).

* Corresponding author at: Dept. of Operating Rooms, 715, P.O. Box 9101, 6500 HB Nijmegen, the Netherlands.
E-mail address: Casper.Tax@radboudumc.nl (C. Tax).

http://dx.doi.org/10.1016/j.ygyno.2015.09.076

Pooled data on a combined tracer in early stage cervical cancer patients with primary tumor size <20 mm (6 studies; 276 patients) resulted in 87% bilateral SLN detection.

Conclusions. Early stage cervical cancer patients (FIGO IA2, IB1, IIA primary tumor size <40 mm) who have no suspicious pre-, and per-operative lymph nodes, and have bilateral negative SLNs after ultra staging, have a residual risk of 0.08% (1/1257) on occult metastases. On the basis of these results we recommend not to perform a full PLND in these patients.

Contents

1. Introduction

Cervical cancer is the fourth most common cancer in women worldwide. With an estimated 266,000 deaths worldwide, it accounts for 7.5% of all female cancer deaths [1]. Pelvic lymph node (PLN) status is an important prognostic factor in cervical cancer, but it is also very important in treatment decisions. The 5-year survival rate decreases from 92% to 64% in case of positive pelvic lymph nodes (PLN), regardless of FIGO stage [2,3]. Guidelines recommend a pelvic lymph node dissection (PLND) in early stage (FIGO IA2, IB1, IIA) cervical cancer in order to detect metastases and adjust treatment accordingly. Only in stage 1A1 disease without lymphovascular space invasion (LVSI) PLND is not recommended because of its low risk of lymph node metastases (<1%) [4]. Lymph node metastases are present in up to 27% in early stage cervical cancer (FIGO stage 1A2–IIA), therefore at least three out of four patients may undergo unnecessary PLND with subsequent risk of significant morbidity and decreased quality of life [2,3,5,6]. A sentinel lymph node (SLN) procedure may detect metastases accurately and may therefore be an attractive alternative to standard PLND.

SLN detection is a standard of care diagnostic procedure for several other tumors like breast, penile, skin and vulvar cancer. It is used as an alternative to a full lymph node dissection in case of a negative SLN [7–9]. The ability to safely predict absence and presence of metastases and therefore replace a full pelvic lymph node dissection will depend on both the detection rate (DR) and the diagnostic accuracy of the SLN procedure. In cervical cancer, there is ongoing debate with regard to whether detection should be bilateral or per pelvis side in order to omit PLND on either side, whether a single tracer or a double tracer (dye and/or radioisotope) should be used, and whether or not the SLN should undergo ultra staging. FIGO stage and tumor size appeared to be important factors influencing both the diagnostic accuracy and detection rate [10–12]. Furthermore, recent reviews on the sentinel lymph node (SLN) procedure in cervical cancer have shown that bilateral SLN detection and ultra staging are safe and superior options compared to a unilateral detection, frozen section and H&E analysis [13,14]. So far, nobody identified a subgroup of patients with clear and applicable criteria in whom a SLN procedure may replace pelvic lymph node dissection (PLND). This appears to preclude the SLN procedure from becoming an alternative to standard pelvic lymph node dissection in early stage cervical cancer patients.

The aim of this diagnostic review therefore is to assess which technique or combination of techniques yields the highest detection rate and diagnostic accuracy for SLN analysis, and to study whether it is possible to identify a subgroup of early cervical cancer patients in which a SLN procedure is a safe alternative to PLND.

2. Materials and methods

2.1. Data sources and searches

We systematically searched Medline, EMBASE, Cochrane Library and CINAHL from inception up to November 26, 2014 for studies on SLN procedure in patients with cervical cancer. The search query combined synonyms for 'cervical cancer' with synonyms for 'sentinel node procedure' (see Supplementary material 1 for the complete search strategy). We also performed a reference and related article search. Duplicate articles were manually filtered using the bibliographic database of EndNote [15].