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Review article

Nerve-sparing radical hysterectomy versus conventional radical hysterectomy in early-stage cervical cancer. A systematic review and meta-analysis of survival and quality of life

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ABSTRACT

Background and aims: Survival after radical hysterectomy (RH) for early-stage cervical cancer is good. Hence quality of life (QOL) after treatment is an important issue. Nerve-sparing radical hysterectomy (NSRH) improves QOL by selectively sparing innervation of bladder, bowel and vagina, reducing therapy-induced morbidity. However, the oncological outcome and the functional outcome after NSRH are subjects of debate. We aim to present the best possible evidence available regarding both QOL and survival after NSRH in early-stage cervical cancer.
Methods: Systematic review and meta-analysis on studies comparing NSRH and RH.
Results: Forty-one studies were included, and 27 were used for the meta-analysis. There was no difference in 2-, 3- and 5-year overall survival: the risk ratios (RRs) were respectively 1.02 (95% CI 0.99–1.05, n = 879), 1.01 (95% CI 0.95–1.08, n = 1324) and 1.03 (95% CI 0.99–1.08, n = 638). No difference was found in 2-, 3- and 5-year disease-free survival: RR 1.01 (95% CI 0.95–1.05, n = 1175), 0.99 (95% CI 0.94–1.03, n = 1130) and 1.00 (95% CI 0.95–1.06, n = 933) respectively. Post-operative time to micturition was significantly shorter in the NSRH group: standardized mean difference (SMD) −0.84 (CI 95% −1.07 to −0.60).
Conclusions: NSRH can be considered safe and effective for early-stage cervical cancer since short- and long-term survival do not differ from those of conventional RH, while bladder function after NSRH is significantly less impaired.

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1. Introduction

Cervical cancer is the third most common type of cancer in women worldwide. Furthermore, it is the fourth most lethal type of cancer in women after breast-, lung and colon carcinoma [1]. In 2010 453,970 new patients were diagnosed with cervical cancer worldwide and 44% of these women were under the age of 50. Only 24% of the cases concerned women from developed countries. Treatment of cervical cancer depends on the stage of the disease. Microscopic disease (FIGO IA1) is usually treated with a cone biopsy or simple hysterectomy. So called 'early stage cervical cancer' (FIGO IA2, IB, IIA and IIB) is usually treated with a radical hysterectomy: depending on the radicality (classified according to Piver I–IV) both the sacro-uterine ligaments and the parametria are resected more extensively but usually the parametrium is resected up to the internal iliac artery and down to the deep uterine vein [2]. In order to rule out lymph node metastasis, a pelvic lymphadenectomy is performed. Adjuvant (chemo-) radiation is administered in case of lymph node metastasis, extra cervical spread and unfavourable tumour characteristics. Prognosis after RH depends on the aforementioned prognostic factors. Five-year survival rates of between 88% and 97% have been reported [3,4]. Given such survival rates, quality of life after treatment is an important issue. One way to improve quality of life is by reducing therapy-induced morbidity. Up to 25% of women treated with radical hysterectomy suffer from bladder, bowel and sexual complaints [5,6]. Maas et al. showed that conventional radical hysterectomy (Piver III) inevitably results in damage to the autonomic nerves in both the hypogastric plexus (resection of the sacro-uterine ligaments) and the splanchnic nerves (resection of the parametrium below the deep uterine vein) [7]. The autonomic nerves innervate the bowel and are important for optimal sexual function: the autonomic nerves regulate lubrication-swelling response of the female genitals during sexual arousal [8]. It is well known that accidental damage to thesenerves in the pelvis can lead to urine incontinence, diarrhoea or constipation and sexual problems [9]. In the 1960s the Japanese gynaecologist Kobayasi described the first technique to conserve the autonomic nerves during pelvic surgery. In 1988 Sakamoto published the first article on nerve-sparing radical hysterectomy (NSRH) in English [7,10]. From that time many different techniques to spare the autonomic nerves in radical hysterectomy have been published and more recently reviews on nerve sparing radical hysterectomy summarised the evidence on the oncological safety of nerve sparing radical hysterectomy [3,4,11]. However nerve-sparing surgery is still subject to a fierce debate in the world of gynaecologic oncology. Proponents state the technique is safe and beneficial for the quality of life of patients. Opponents are reluctant to use the technique arguing that literature is too heterogeneous to be certain about both oncological safety and anatomical and physiological advantage. In this meta-analysis, of the data obtained after systematically reviewing all available literature, we aim to provide the best possible evidence available regarding both quality of life and survival after NSRH in early stage cervical cancer. Since none of the aforementioned reviews performed a proper meta-analysis to the extent as we did, our paper will hopefully close the debate in favour of the effect and safe use of NSRH. This will allow women to undergo the most optimal surgical treatment for early stage cervical cancer.

2. Materials and methods

2.1. Definitions

Early stage cervical cancer includes stage IA2, IB, IIA and IIB cervical cancer according to the Féderation Internationale de Gynécologie et d'Obstétrique (FIGO) staging [12]. The intervention under review is nerve sparing radical hysterectomy (NSRH), which is compared to conventional radical hysterectomy (RH). The PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-analyses) were used during the development and execution of this systematic review and meta-analyses.

2.2. Sources

We searched PubMed, EMBASE, Web of Science, the Cochrane Library, CINAHL, Academic Search Premier, ScienceDirect, Springer, WileyBlackwell, LWW, HighWire and Taylor & Francis/Informaworld (final search November 21st 2015). The following terms with synonyms were used: (radical) hysterectomy, nerve-sparing, cervical cancer and autonomic nerves. Supplemental Fig. 1 shows the exact search strategy. (S1 search specifics) A single librarian of the Waleaus library of the Leiden University Medical Center (JS) performed the literature searches.

2.3. Study selection

We included case-control studies, randomised controlled trials and comparative cohort studies. To avoid publication bias, no limitations on language or publication date were made. The meta-analyses were performed on the comparative studies. We excluded studies without the definition of cervical cancer or nerve sparing surgery. Four independent reviewers (M.v.G, L.R., K.v.S and C.d.K) screened the titles and abstracts. If the title was not specific enough for decision, we reviewed the abstract. If a reference was eligible, the full-text article was scored using a pre-tested scoring list conducted by the reviewers (M.v.G, L.R., K.v.S and C.d.K). Inconsistency between the reviewers was resolved by discussion and consensus. Data were extracted using a pre-designed data extraction form. Hence both methodology and results of all eligible papers were