Summary

This thesis aims to evaluate the different aspects of niches in the uterine caesarean scar. This chapter summarises the results of the research we conducted.

In the introduction in chapter one the background and the different aspects of a niche are outlined. The caesarean section (CS) rate is increasing and long term effects of caesarean scars are getting more attention now that more women have had a previous CS. A niche is mainly a sonographic finding and has been defined as a triangular anechoic area at the presumed site of incision. Although a uniform definition of a niche is still under debate, Niches have been related to bleeding disorders. Studies on the prevalence of niches in a more or less random population or prospective studies relating niches with bleeding disorders were lacking. Also studies in which niches are evaluated by hysteroscopy were only performed in symptomatic patients. There is no information on the natural development of the uterine scar over a period in time. Although studies have been performed to identify risk factors prospective studies are lacking. Different surgical therapies have been proposed for the treatment of niche related symptoms although the effectiveness of these therapies are under debate.

The aim of this thesis is formulated in five main questions.

- What is the prevalence of a niche after a CS (chapter 2, 3, 5)
- Does a uterine caesarean scar change over time (chapter 4)
- Is there a relationship between a niche and post menstrual spotting or urologic symptoms (chapter 3)
- What are risk factors for developing a niche (chapter 6)
- How to treat niche related symptoms? (chapter 7, 8, 9)

In chapter two a systematic overview of the available literature on the prevalence of a niche using various diagnostic methods, on potential risk factors for the development of a niche and on niche-related gynecological symptoms in non-pregnant women are given. In total 21 papers were included. Niche prevalence varied dependent on the method used, the definition used and the study population. With trans vaginal ultrasound (TVU) the prevalence in a random population varies between 24% and 70%, using sonohysterography (SHG) in a random population the prevalence varies between 56%-84%. The prevalence of niches evaluated with hysteroscopy was performed in symptomatic women only. Possible risk factors were one layer closure of the uterus, multiple CS and retroflexed uterus. The predominating symptom related to a niche was post menstrual spotting (brownish discharge after menstruation has ended).

The limitation of this review was a lack of consistency in the methodology of the papers we indentified. This was based on three aspects. First of all there was no generally accepted definition of a niche or a large niche. Secondly different methods were used to identify a niche. Finally the studies were performed in a significant heterogenic population of women with and without symptoms and with one or more previous caesarean sections.
In chapter three we studied the prevalence of niches in an asymptomatic population and the relationship with post menstrual spotting and urological incontinence. In a prospective observational cohort study including 263 women we found 49.6% niches by TVU and 64.5% by gel installation sonohysterography (GIS) at 6-12 weeks after CS. Women were followed by questionnaire and pictorial charts at 6-12 weeks, 6 months and 12 months after CS. One year after CS women with a niche, measured by GIS, reported more postmenstrual spotting than women without a niche (OR 5.48, 95% CI 1.14–26.48). Women with a ratio of residual myometrium/adjacent myometrium < 50 % reported more post menstrual spotting. (OR 6.13, 95% CI 1.74–21.63). Urinary incontinence was not related to the presence of a niche. We proposed that GIS is in favour over TVU for niche evaluation including the measurement of the residual myometrium thickness (RMT).

In chapter four we reported the results of a prospective longitudinal study on the changes occurring in an uterine scar the first year after a CS. Women with one previous CS were evaluated with both TVU and GIS at 2 and 12 months after the CS. We found that the prevalence of niches did not change but RMT decrease independent of the method used. With GIS mean RMT changed in time from 11.9 mm at 2 months to 6.5 mm at 12 months after the CS (p<0.001) The adjacent myometrium reduced from 15 mm to 12.4 mm (p=0.04) The ratio between RMT and AM with GIS decreased from 0.80 at 2 months to 0.64 at 12 months (p=0.002). The uterine scar is not a static feature and does change in time. This has to be taken in account in timing of niche measurement.

In chapter five we evaluated the prevalence of niches by hysteroscopy and designed a registration form for the evaluation of niches by hysteroscopy. We compared women with (n=110) and without (n=603) a previous CS seeking sterilisation by hysteroscopic tubal occlusion in a prospective cohort study. The hysteroscopic features of the anterior wall and the prevalence of niches was evaluated by 5 mm hysteroscopy. A niche was defined as any visible defect, disruption, or concavity (gap) in the anterior wall. Eigthy-three (75%) niches were observed in women with a previous CS and no defects in women without a previous CS. Based on the evaluated features of a niche we developed a registration form including the following items; polyps, cysts, myometrium defect, fibrotic tissue, (abnormal) vascular pattern, lateral branches, mucus production inside the defect, and bleeding.

In chapter six the outcomes of the identification of risk factors and the development of a prognostic model for the development of a niche in the uterine caesarean scar are described. In a prospective cohort study including 134 women with one previous CS who were evaluated by GIS 6-12 weeks after CS a prognostic model was developed. A niche was defined as an indentation with a depth of at least 2mm. A large niche was defined as a niche with a depth of at least 5mm. After backwards multivariable logistic regression analysis and multiple imputation the following prognostic factors were identified; cervical dilatation 4-7 cm (OR 8.93 [95% CI 1.89-42.19]), cervical dilatation 8-10 cm (OR 9.26 [95% CI 1.88-45.94]) and induction of labour (OR 4.76 [95% CI 1.25-18.21] increased the risk...
of the development of a niche while contractions before CS (OR .114 [95% CI .023-.570]) prevents niche development. Based on these risk factors we postulated the hypothesis that the development of the low uterine segment and the position of the uterine incision are of influence for developing a niche.

The model designed with these factors had a low predictive value, underlying the fact that niche development is multifactorial and indicates that we miss relevant factors in our study that should be included in future studies.

A systematic review on minimal invasive therapy to treat niche related symptoms is presented in chapter seven. In this review twelve studies were included. To be included they had to report on one of the following outcomes: effect on abnormal uterine bleeding, pain relief, sexual function, quality of life, and surgical, anatomic, fertility, or pregnancy outcome. The included studies reported on hysteroscopic niche resection (eight studies, 384 patients), laparoscopic repair (one study, 13 patients), (laparoscopic assisted) vaginal repair (two studies, 47 patients), and oral contraceptives (OCs) (one study, 11 patients). In 87% - 100% of women the abnormal uterine bleeding was reported to be improved after these interventions. Sample sizes and follow-up were insufficient to study fertility or pregnancy outcome. Reported complication rates were low. The methodological quality of the selected papers was considered to be moderate to poor, and therefore more evidence is needed before these interventions are implemented in daily practise.

In chapter eight the study protocol is presented of a multicenter randomised controlled trial to evaluate the (cost) effectiveness of hysteroscopic niche resection on post menstrual spotting and quality of life, the HysNiche trial. Women with ≥ 2 days of post menstrual spotting and a niche with a depth of at least 2 mm and a residual myometrium thickness ≥3 mm were randomly assigned to hysteroscopic resection or expectant management for six months. Primary outcome were days of postmenstrual spotting at 6 months after randomisation. Secondary outcomes were menstruation aspects, experienced discomfort and satisfaction, quality of life, sexual function, urinary symptoms, absence from work, medical consultation, medication use and received additional therapies (diary) at 3 and 6 months after randomisation. We aimed to include 100 women. This study was performed in the Dutch Consortium for Studies in Women’s Health and Reproduction.

Chapter nine presents the results of the HysNiche trial. One hundred and three patients were randomised between hysteroscopic resection (n=52) or expected management (n=51) and of 51 and 44 women respectively the outcome was available at six months after randomisation.

Six months after randomisation the mean days of postmenstrual spotting reduced with 4 days (IQR 2-7) in the intervention group compared to 1 day (IQR3-10) in the control group at 6 months follow-up (p=0.04). Median discomfort related to spotting on a scale of 0 to 10 reduced from 8 at baseline to 2.0 (IQR 0– 6.8) in the intervention group and from 8 to
6.9 (IQR 0.4–8.0) in the control group (p=0.02) at six months. Significant more women received additional surgical interventions during the first 6 months follow-up in the expectant management group due to persisting spotting symptoms.

Chapter ten provides a summary of the main findings in English and Dutch.

In chapter eleven the results of this thesis are discussed, clinical implications are addressed and implications for further research are provided.