Diagnostic and prognostic aspects of tubal patency testing

Coppus, S.F.P.J.

Citation for published version (APA):
Coppus, S. F. P. J. (2012). Diagnostic and prognostic aspects of tubal patency testing.
The capacity of hysterosalpingography and laparoscopy to predict natural conception.

Harold Verhoeve
Sjors Coppus
Jan Willem van der Steeg
Pieternel Steures
Peter Hompes
Petra Bourdrez
Patrick Bossuyt
Fulco van der Veen
Ben Willem Mol

*Human Reproduction* 2011, 26: 134-142

The contents of this article were presented as a poster presentation at the 63rd ASRM Annual Meeting, 2007, Washington, USA.
Abstract

BACKGROUND: Laparoscopy has been claimed to be superior to hysterosalpingography (HSG) in predicting fertility. Whether this conclusion is applicable to a general subfertile population can be questioned as data in support of this claim were collected in third line centres. The aim of this study was to assess the prognostic capacity of HSG and laparoscopy in a general subfertile population.

METHODS: In 38 centres, we prospectively studied a cohort of patients referred for subfertility between 2002 and 2004, who underwent HSG and/or laparoscopy as part of their subfertility work-up. Follow-up started immediately after tubal testing and ended 12 months thereafter. Time to pregnancy was censored at the date of last contact, when the woman was not pregnant or at the start of treatment. Kaplan-Meier curves for the occurrence of spontaneous intrauterine pregnancy were constructed for patients without tubal pathology, for those with unilateral tubal pathology and for patients with bilateral tubal pathology at HSG or laparoscopy. Multivariable Cox regression analysis was used to calculate fecundity rate ratios (FRRs) to express associations between tubal pathology and the occurrence of an intrauterine pregnancy.

RESULTS: Of the 3301 included patients, 2043 underwent HSG only, 747 underwent diagnostic laparoscopy only and 511 underwent both. At HSG, 322 (13%) patients showed unilateral tubal pathology and 135 (5%) showed bilateral tubal pathology. At laparoscopy, 167 (13%) showed unilateral tubal pathology and 215 (17%) showed bilateral tubal pathology. Multivariable analysis resulted in FRRs of 0.81 (95% confidence interval (CI): 0.59-1.1) for unilateral, and 0.28 (95% CI: 0.13-0.59) for bilateral, tubal pathology at HSG. The FRRs at laparoscopy were 0.85 (95% CI: 0.47-1.52) for unilateral, and 0.24 (95% CI: 0.11-0.54) for bilateral, tubal pathology.

CONCLUSIONS: Patients with unilateral tubal pathology at HSG or laparoscopy had a moderate reduction in pregnancy chances, whereas those with bilateral tubal pathology at HSG or laparoscopy had a severe reduction in pregnancy chances. This reduction was similar for HSG and laparoscopy, suggesting that HSG and laparoscopy have a comparable predictive capacity for natural conception.
Prognostic significance of HSG and laparoscopy

Introduction

The prevalence of tubal pathology in subfertile populations varies between 11 and 30% and depends on whether one deals with a population in a primary, secondary or tertiary setting, with the lowest prevalence in a primary care setting (Hull et al., 1985; Collins et al., 1995; Snick et al., 1997). *Chlamydia trachomatis* is a major cause for tubal pathology. *Chlamydia* infection is often asymptomatic and untreated *Chlamydia* can progress to pelvic inflammatory disease (PID), infertility, ectopic pregnancy, and chronic pelvic pain. An increase in the prevalence of *Chlamydia* infections has been observed in women in their reproductive phase of life (Rekart and Brunham, 2008) and hence tubal pathology remains an important cause of subfertility.

A number of diagnostic tests are being used in clinical practice to assess tubal patency as part of the work-up for subfertility. The most commonly used tests are hysterosalpingography (HSG) and laparoscopy. HSG and *Chlamydia Antibody Titer* test (CAT) are often seen as screening tests for the presence of tubal pathology (den Hartog et al., 2008), whereas laparoscopy is considered the clinical reference test for diagnosing tubal pathology (Swart et al., 1995; Mol et al., 1999b). Laparoscopy allows visualization of peri-adenosal adhesions and the presence of endometriosis, which cannot be done with HSG. Because of their invasive nature, HSG and laparoscopy are usually reserved as the last investigation in the fertility work-up. The findings at these diagnostic tests should translate into a prognosis of natural pregnancy chances, which can be used to counsel patients on whether their pregnancy chances can be improved by surgery, IUI or IVF.

The relative merits of HSG and laparoscopy for assessing tubal status have been discussed for many years, reflecting a lack of agreement amongst fertility subspecialists on which diagnostic tests have to be performed and their prognostic utility (Helmerhorst et al., 1995; Balash, 2000; Fatum et al., 2002; Lavy et al., 2004; Perquin et al., 2006).

Some studies have shown that patients with unilateral tubal pathology at HSG do not have reduced chances of a treatment-independent pregnancy, in contrast to those with bilateral tubal pathology (Mol et al., 1997). For diagnostic laparoscopy (DLS) and dye, a moderate reduction of natural pregnancy chances in case
of unilateral tubal pathology and a severe reduction in case of bilateral tubal pathology have been observed (Mol et al., 1999a). However these studies were retrospective in design, relatively small and had included patients visiting a tertiary referral hospital. In another study, laparoscopy was found to be a better predictor of future fertility than HSG (Mol et al., 1999b). This study analysed data of couples who underwent both HSG and laparoscopy and also consisted of a tertiary care population. The conclusion that laparoscopy is a better predictor of infertility than HSG was weakened by the fact that the median interval to laparoscopy after a normal HSG was 10 months, compared with 4.5 months for women in whom the HSG showed two-sided tubal abnormalities.

It is not clear if the results of these studies are applicable to the general subfertile population. The purpose of the study presented here was to evaluate the impact of unilateral and bilateral tubal pathology at HSG and laparoscopy on treatment-independent pregnancy rates in a large prospective cohort of subfertile ovulatory women from mixed secondary and tertiary hospital population. In particular, we evaluated whether a difference in prognostic capacity exists between HSG and laparoscopy.

**Materials and Methods**

Between January 2002 and February 2004, consecutive couples presenting at the fertility clinic of 38 centres in The Netherlands were asked to participate in a prospective cohort study. The study was approved by the Institutional Review Board in each institution. All couples underwent a basic fertility work-up according to the guidelines of the Dutch Society of Obstetrics and Gynaecology. The details of this work-up have been described previously (van der Steeg et al., 2007).

**Patients**

The present analysis was limited to couples with a regular ovulatory cycle, defined as a cycle length between 23 and 35 days, with a within cycle variation of less than 8 days. None of the patients analysed used Clomiphene Citrate. Ovulation was detected by a basal body temperature chart, midluteal serum progesterone, or by ultrasonographic monitoring of the cycle. Couples with a history of reversal of sterilization, tubal surgery, IVF, or previous tubal patency testing were excluded.
Only those women who underwent HSG and/or laparoscopy as part of their fertility work-up were included in the analysis presented here.

Duration of subfertility was defined as the period between the time the couple had started trying to conceive and the time of tubal testing. Female age was calculated at the time of HSG or laparoscopy. Subfertility was considered to be secondary if a woman had conceived in this or in a previous partnership, regardless of the pregnancy outcome.

In all male partners, at least one semen analysis was performed. The total motile sperm count (TMC) was calculated by multiplying semen volume, sperm concentration and percentage of motile spermatozoa. Couples in whom semen analysis showed a severe impairment of semen quality requiring IVF-ICSI (defined as a total motile count < 1*10⁶), were also excluded from the present analysis.

**Tubal testing and follow-up**
Clinics were free to use their own tubal testing protocol. In general, three different protocols could be distinguished. With the first strategy, tubal patency was routinely evaluated early in the work-up with either HSG or laparoscopy. In case of abnormal findings at HSG, a laparoscopy was planned to verify these findings. With the second strategy, tubal pathology was considered to be absent in case of a negative CAT and HSG or laparoscopy was only performed in CAT-positive women. With the third strategy, CAT-negative women were evaluated with HSG, while laparoscopy was planned in CAT-positive women.

HSG was performed in the follicular phase of the menstrual cycle with either a water-soluble or oil-based contrast medium. Patients were in a supine position during the whole procedure. X-ray photographs were taken. Spasmolytic drugs were allowed to be used. Each HSG was evaluated by a fertility specialist. Laparoscopy was performed with a double-puncture technique. Methylene blue was injected at room temperature through a Foley catheter in the uterine cavity. The amount of methylene blue injected was variable, depending on the time necessary to assess tubal function. Findings at HSG were classified as no tubal occlusion, one-sided tubal occlusion or two-sided tubal occlusion and impaired flow of contrast if contrast was not shown beyond the isthmic portion of the tube. Findings at laparoscopy were classified as normal, one-sided tubal occlusion or
two-sided tubal occlusion and proximal- or distal tubal occlusion. Additional tubal pathology at laparoscopy, i.e. adhesions disturbing ovum pick-up were classified separately.

Follow-up started after tubal testing and ended 12 months thereafter. A model was used to calculate the chances of natural conception (Hunault et al., 2004). Expectant management was advised if the fertility work-up showed no abnormalities and couples had a probability of natural conception in the next 12 months of 40% or higher. Treatment was generally advised to those with a probability below 30%. For all women lost to follow-up, the general practitioner was sent a questionnaire and asked about the fertility status of the couple.

Analysis
The primary end-point in this study was a spontaneous ongoing pregnancy at 12 weeks of gestational age, confirmed by ultrasonography. The first day of the last menstrual cycle was considered to mark the end of time until spontaneous conception. Time to pregnancy was censored at the moment treatment (IUI, IVF or tubal surgery) started within 12 months after counseling, or at the last date of contact during follow-up, when the couple had no ongoing pregnancy.

To examine if proximal occlusions identified at HSG or laparoscopy had a different prognostic effect on treatment-independent pregnancy than distal occlusion / hydrosalpinx or hydrosalpinges, ongoing pregnancy rates were scored in relation to the findings of tubal testing at HSG and laparoscopy. We classified the findings at HSG and laparoscopy into three groups and constructed Kaplan-Meier curves for each i.e. for women without tubal pathology, for those with one-sided tubal pathology and for women with two-sided tubal pathology, irrespective of their nature. Subsequently, adjusted fecundity rate ratios (FRRs) and 95% confidence intervals (CIs) were calculated through multivariable Cox regression modeling. These FRRs express the instantaneous probability of an ongoing pregnancy for women with a particular feature relative to the probability in those without that feature. All analyses were stratified according to centre, to adjust for any potential clustering effects of type of tubal work-up and for differences in prognostic profile of women presenting to the participating clinics (Harrell, 2001).
In case a woman had been evaluated both with HSG and DLS, the results of these were evaluated separately, i.e. the result of the respective tubal test was used in the analysis, not the definitive diagnosis regarding tubal pathology in an individual woman. In those women who underwent both HSG and laparoscopy, we classified tubal pathology as no abnormalities, unilateral pathology and bilateral pathology and subsequently constructed 3 x 3 tables to compare tubal occlusion detected at HSG with occlusion detected at laparoscopy.

Results

Data of 7860 couples were collected. Of these, 938 women (12%) did not have a regular ovulatory cycle, 636 men (8%) had severely impaired semen quality and 196 couples (2.5%) had previously undergone fertility surgery or IVF. In another 568 women (7%) HSG or laparoscopy had been performed in a previous episode of subfertility. A further 2221 women (28%) did not undergo HSG or DLS as part of their fertility work-up, leaving 3301 women (42%) for this analysis (Fig. 1).

The baseline characteristics of the 3301 couples are shown in Table I. Median duration of subfertility at HSG was 1.8 years (5th-95th percentiles: 1.0-4.3 years) and at laparoscopy 2.2 years (5th-95th percentiles: 1.2-5.0 years). The median time from the first visit to HSG was 3.0 months (5th-95th percentiles: 1-11.4), the median time from the first visit to laparoscopy was 5.9 months (5th-95th percentile: 1.4-16.8). Of the 3301 women in the analysis, 2043 underwent HSG, 747 women underwent DLS and in 511 women the tubal status was evaluated with both.

In 1626 of the HSGs (64%) a water-based contrast medium was used and in 359 of the HSG’s (14%) an oil-based contrast medium was used; in 569 (22%) it was unknown which medium was used. The findings at HSG and laparoscopy and occurrence of ongoing pregnancies are shown in Tables II and III. The data we collected allowed us to make a distinction between proximal and distal occlusion/hydrosalpinx for laparoscopy. In the collected data for HSG, the only distinction we were allowed to make was between no occlusion, occlusion and impaired flow of contrast, by which was meant the absence of flow of contrast beyond the isthmic portion of the fallopian tube. No distinction could be made between proximal and distal occlusion.
TABLE I. Baseline characteristics of 3301 couples at time of procedure

<table>
<thead>
<tr>
<th></th>
<th>HSG (n=2554)</th>
<th>Diagnostic laparoscopy (n=1258)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean/Median*</td>
<td>5th-95th percentiles</td>
</tr>
<tr>
<td>Male age (years)</td>
<td>35.4</td>
<td>28.0 – 45.0</td>
</tr>
<tr>
<td>Duration of subfertility (years)</td>
<td>1.8*</td>
<td>1.0 – 4.3</td>
</tr>
<tr>
<td>Semen analysis – TMC (10^6)</td>
<td>57.6*</td>
<td>4.0 – 308</td>
</tr>
<tr>
<td>Subfertility, primary (n) (%)</td>
<td>1568</td>
<td>61.4</td>
</tr>
<tr>
<td>Time to tubal test (months)†</td>
<td>3.0*</td>
<td>1.0-11.4</td>
</tr>
</tbody>
</table>

TMC, total motile sperm count.
*Value is the median.
† time from first consultation to tubal testing

Of the women who had a HSG, 186 (7%) were lost to follow-up and of those who had a laparoscopy 88 (7%) were lost to follow-up. A natural conception within one year occurred in 454 (18%) of the women after HSG, in 126 (10%) after laparoscopy and in 48 (9.4%) of those who underwent both HSG and laparoscopy, which would correspond with cumulative treatment-independent pregnancy rates of 33% after HSG and 23% after laparoscopy (Fig. 2). The number of patients, who were still under study at 6 and 12 months, respectively was 800 and 240 after HSG. For laparoscopy these numbers were 243 and 81, respectively. In those with unilateral tubal pathology, these numbers were 145 and 57 after HSG and 46 and 14 after laparoscopy. For patients with bilateral tubal pathology, the numbers remaining for analysis at 6 and 12 months were 68 and 20 after HSG in comparison to 74 and 24 after laparoscopy.

TABLE II. Fertility outcome after HSG

<table>
<thead>
<tr>
<th>Findings at HSG</th>
<th>Frequency (%)</th>
<th>Number of ongoing pregnancies</th>
<th>FRR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral normal</td>
<td>2097 (82%)</td>
<td>350</td>
<td>1</td>
</tr>
<tr>
<td>Unilateral impaired flow of contrast *</td>
<td>84 (3%)</td>
<td>10</td>
<td>0.68 (0.36-1.3)</td>
</tr>
<tr>
<td>Unilateral occlusion</td>
<td>238 (9%)</td>
<td>38</td>
<td>0.89 (0.63-1.3)</td>
</tr>
<tr>
<td>Unilateral occlusion, contra-lateral impaired flow of contrast*</td>
<td>25 (1%)</td>
<td>2</td>
<td>0.36 (0.09-1.5)</td>
</tr>
<tr>
<td>Bilateral impaired flow of contrast*</td>
<td>51 (2%)</td>
<td>2</td>
<td>0.19 (0.05-0.80)</td>
</tr>
<tr>
<td>Bilateral occlusion</td>
<td>59 (2%)</td>
<td>3</td>
<td>0.26 (0.08-0.80)</td>
</tr>
</tbody>
</table>

FRR = Fecundity Rate Ratio
*Impaired flow meaning no flow of contrast beyond the isthmic portion of the tube.

In 511 patients both HSG and laparoscopy were performed. Tubal status detected at HSG compared to tubal status detected at laparoscopy is shown in table IV. HSG showed one-sided tubal occlusion in 153 (30%) and two-sided tubal occlusion
in 82 (16%) of these patients. Laparoscopy showed one-sided tubal occlusion in 79 (15%) and two-sided tubal occlusion in 56 (11%) of these patients. In those patients where HSG showed one-sided occlusion, laparoscopy revealed no occlusion in 60%, whereas if HSG showed two-sided occlusion, laparoscopy revealed no occlusion in 44%. If laparoscopy showed one-sided occlusion, HSG revealed no occlusion in 22% of these patients and if laparoscopy showed two-sided occlusion, HSG showed no occlusion in 23% of cases.

TABLE III. Fertility outcome after laparoscopy.

<table>
<thead>
<tr>
<th>Findings at laparoscopy</th>
<th>Frequency (%)</th>
<th>Number of ongoing pregnancies</th>
<th>FRR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral normal</td>
<td>876 (70%)</td>
<td>90</td>
<td>1</td>
</tr>
<tr>
<td>Unilateral proximal occlusion</td>
<td>126 (10%)</td>
<td>12</td>
<td>0.58 (0.44-1.7)</td>
</tr>
<tr>
<td>Unilateral hydrosalpinx/distal occlusion</td>
<td>25 (2%)</td>
<td>3</td>
<td>1.40 (0.43-4.5)</td>
</tr>
<tr>
<td>Unilateral proximal occlusion, contralateral hydrosalpinx/distal occlusion</td>
<td>21 (2%)</td>
<td>3</td>
<td>1.83 (0.56-6.0)</td>
</tr>
<tr>
<td>Bilateral proximal occlusion</td>
<td>114 (9%)</td>
<td>3</td>
<td>0.19 (0.06-0.62)</td>
</tr>
<tr>
<td>Bilateral hydrosalpinx/distal occlusion</td>
<td>23 (2%)</td>
<td>1</td>
<td>0.34 (0.05-2.5)</td>
</tr>
<tr>
<td>Unilateral proximal occlusion/ hydrosalpinx/distal occlusion, contra-lateral adhesions</td>
<td>32 (3%)</td>
<td>1</td>
<td>0.58 (0.08-4.4)</td>
</tr>
<tr>
<td>Bilateral patent, unilateral adhesions</td>
<td>16 (1%)</td>
<td>0</td>
<td>0 (0-NE)</td>
</tr>
<tr>
<td>Bilateral patent, bilateral adhesions</td>
<td>25 (2%)</td>
<td>0</td>
<td>0 (0-NE)</td>
</tr>
</tbody>
</table>

FRR = Fecundity Rate Ratio
NE = not estimable

After HSG, the presence of unilateral impaired flow and unilateral occlusion showed no significant difference in FRR (0.68 and 0.89, respectively, with wide and overlapping CIs). Similarly, a small difference in FRR (0.19 and 0.26) between bilateral impaired flow and occlusion (which included proximal and distal occlusion) was seen (table II). For this reason impaired flow of contrast was considered as complete occlusion, because this did not prove tubal patency.

With laparoscopy, we found no differences in prognostic outcome for proximal occlusions identified at laparoscopy compared with distal occlusion / hydrosalpinx or hydrosalpinges. For unilateral proximal occlusion the FRR was 0.58 and for distal unilateral occlusion 1.40, but both showed wide and overlapping CIs. For bilateral proximal occlusion the FRR was 0.19 compared to 0.34 in case of bilateral distal occlusion, with a wide and overlapping CI in the latter (Table III). We therefore classified tubal pathology into three main categories, namely no tubal pathology, unilateral tubal pathology and bilateral tubal pathology.
Using this classification, the results of the uni- and multivariable Cox regression analysis are shown in Table V. At HSG the prevalence of one-sided tubal pathology was 13% (322 women), and of bilateral tubal pathology 5.3% (135 women). At laparoscopy, the prevalence of one-sided tubal pathology was 13% (167 women) and of bilateral tubal pathology 17% (215 women).

### TABLE IV. Tubal status detected at HSG as compared to the tubal status detected at laparoscopy.

<table>
<thead>
<tr>
<th></th>
<th>Laparoscopy</th>
<th>Two-sided occlusion</th>
<th>One-sided occlusion</th>
<th>No occlusion</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSG</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Two-sided occlusion</td>
<td>31</td>
<td>15</td>
<td>36</td>
<td>82</td>
<td></td>
</tr>
<tr>
<td>One-sided occlusion</td>
<td>12</td>
<td>47</td>
<td>94</td>
<td>153</td>
<td></td>
</tr>
<tr>
<td>No occlusion</td>
<td>13</td>
<td>17</td>
<td>246</td>
<td>276</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>56</td>
<td>79</td>
<td>376</td>
<td>511</td>
<td></td>
</tr>
</tbody>
</table>

Bilateral tubal pathology at HSG or laparoscopy was associated with a lower probability of treatment-independent pregnancy, with an adjusted FRR of 0.28 (95% CI: 0.13-0.59) for HSG and 0.24 (95% CI: 0.11-0.54) for laparoscopy. Unilateral tubal pathology at HSG or laparoscopy affected the probability of treatment-independent pregnancy slightly, with an adjusted FRR of 0.81 (95% CI: 0.59-1.11) for HSG and 0.85 (95% CI: 0.47-1.52) for laparoscopy. A comparable reduction in the probability of treatment-independent pregnancy was seen for duration of subfertility with a FRR of 0.90 (95% CI: 0.90 to 1.00) and 0.78 (95% CI: 0.64 to 0.95) for HSG and laparoscopy respectively. Kaplan-Meier analyses of the cumulative probability of spontaneous intrauterine pregnancy up to 1 year are shown in Fig. 2a for HSG and Fig. 2b for laparoscopy. For HSG the cumulative pregnancy rate after finding unilateral tubal pathology was slightly reduced, but after bilateral tubal pathology the cumulative pregnancy rate was markedly reduced. Similar results were seen for laparoscopy.
FIGURE 2A. Cumulative ongoing pregnancy rate after HSG.

Results of the Kaplan-Meier analysis for HSG. Black line represents bilateral normal HSG. Light grey line represents one-sided abnormal HSG. Dark grey line represents women with a bilateral abnormal HSG. Crosses indicate censored data.

FIGURE 2B. Cumulative ongoing pregnancy rate after laparoscopy.

Results of the Kaplan-Meier analysis for laparoscopy (DLS). Black line represents bilateral normal DLS. Light grey line represents one-sided abnormal DLS. Dark grey line represents women with a bilateral abnormal DLS. Crosses indicate censored data.
Discussion

In this study we compared findings at HSG and laparoscopy with fertility outcome in untreated subfertile couples, from the time of tubal testing up to 1 year of follow-up. For HSG as well as for laparoscopy, patients with two-sided tubal pathology had significantly worse fertility prospects, whereas fertility prospects in those with one-sided tubal pathology were only moderately worse than those without tubal pathology. Both imaging tests showed a comparable reduction in FRRs for unilateral as well as for bilateral tubal pathology.

Because proximal tubal pathology (occlusion as well as impaired flow) is more likely to be due to artefacts, such as tubal spasm or ‘steal effect’ than distal tubal occlusion or hydrosalpinx, we analysed whether there was a difference in FRR between proximal and distal tubal pathology for the detection of natural pregnancy, but we were unable to detect such a difference. For this reason we classified the findings at HSG and laparoscopy into three main groups, namely...
no tubal pathology, unilateral tubal pathology and bilateral tubal pathology to calculate the FRRs.

The fertility rate ratios for two-sided tubal pathology are in accordance with results from our previous small retrospective Dutch cohort study, which examined the prognostic value of HSG for fertility outcome, as well as with data of the previous large prospective Canadian study (Mol et al., 1997, 1999b). However, in the present study we found a lower FRR in case of bilateral tubal pathology at HSG, compared with the Canadian cohort. This could be due to the lower prevalence of bilateral tubal pathology at HSG (5% compared to 24% in the Canadian study) whereas the prevalence of unilateral tubal pathology at HSG was comparable (13% versus 14%). This might be explained by the fact that in the Canadian study only patients that underwent both HSG and laparoscopy were analysed. Patients who had an abnormal HSG but had a natural conception before a laparoscopy was performed were not part of the analysis. Since natural conception indicates absence of significant tubal pathology, a selection of patients with a higher prevalence of tubal pathology took place in this study. Although the present study showed a similarly low FRR for bilateral tubal pathology at laparoscopy, the prognostic value of unilateral tubal pathology identified at laparoscopy (FRR 0.85) differed markedly from that in our previous two studies, which showed a FRR of 0.65 and 0.51 respectively (Mol et al., 1999a,b). Both studies included only women from a tertiary patient population who had a HSG followed by laparoscopy. Laparoscopy was usually performed shortly after an abnormal HSG, whereas for women with a normal HSG the laparoscopy was withheld for a longer time. In the present study, 15% of the patients underwent both HSG and laparoscopy. The median time between the first visit of a couple and laparoscopy was 5.9 months compared to a median time in the Canadian study between HSG and laparoscopy of 10 months in those in whom HSG showed no abnormalities, and 8.5 months in those in whom HSG showed unilateral tubal occlusion and 4.5 months in those in whom HSG showed bilateral tubal occlusion, respectively.

In that study there were relatively few women in whom bilateral occlusion was found at laparoscopy after a normal HSG or one-sided tubal occlusion at HSG (5%) (Mol et al., 1999b). The longer delay between HSG and laparoscopy in the Canadian study resulted in a higher proportion of patients with poor prognosis, which could have negatively influenced the FRR. Selection bias may have influenced
the outcome of these previous studies, overestimating the detection rate of tubal pathology at laparoscopy in comparison to patients who only undergo HSG or a laparoscopy without a previous HSG.

Of notice is the lack of agreement between HSG and laparoscopy in those patients who underwent both imaging tests. At laparoscopy bilateral tubal occlusion was diagnosed in 5% of the patients where previously HSG showed no occlusion. However, in 60% of the patients where HSG showed one-sided occlusion, and in 44% where HSG showed two-sided occlusion, laparoscopy did not show any tubal occlusion. In 23% of the patients with two-sided occlusion at laparoscopy, HSG showed tubal patency, emphasising that laparoscopy cannot be considered the gold standard for diagnosing tubal pathology (Mol et al. 1999b).

Our finding that the presence of tubal pathology at HSG and laparoscopy has a similar FRR is of interest. Unilateral tubal pathology reduced the probability of a natural conception by 20% and bilateral tubal pathology reduced pregnancy chances by 75%, whether diagnosed at HSG or at laparoscopy. Although we were not able to directly compare the prognostic capacity of both imaging tests, because only 15% of the included patients underwent HSG as well as laparoscopy and as there were several months in between these tests, our findings suggest that the prognostic capacity of HSG and that of laparoscopy do not differ much. This is in contrast with previous studies, which concluded that laparoscopy is a better predictor of treatment-independent pregnancy (Mol et al., 1999b).

The results of our study are in support of the recommendation of the fertility-guidelines of the National Institute for Clinical Excellence to use HSG to test for tubal pathology in women who are not known to have co-morbidities (NICE, 2004). Additional advantages of HSG are that a normal HSG reduces the probability that tubal pathology plays a role in future fertility chances, as we can see in this study, and which confirms the findings of previous studies (Swart et al., 1995, Mol et al., 1999b, den Hartog et al., 2008). If an oil-soluble contrast medium is used for tubal flushing, this can have a positive effect on pregnancy rates (Luttjeboer et al., 2007). Using HSG in women at low risk for tubal pathology limits the number of unnecessary laparoscopies because the prevalence of tubal pathology after normal HSG is low (Bosteels et al., 2007, den Hartog et al., 2008). A randomised trial did not show an improved pregnancy outcome if diagnostic laparoscopy
was routinely performed after normal HSG and before treatment with intrauterine insemination (Tanahatoe et al., 2005).

An important limitation of our study is that not in every patient HSG as well as laparoscopy was performed. Patients at low risk for tubal pathology were offered HSG and those with co-morbidities and considered to be at risk for tubal pathology, were offered laparoscopy. Furthermore, the interpretation of this study, like previous studies, is hampered by selection bias caused by a difference in timing of the imaging tests. It is not clear to what extent these limitations influence the outcome of our study. Correction for these requires a study in which women are offered CAT, HSG and laparoscopy as part of their subfertility work-up. These tests should preferably be performed on the same day, or with a minimal delay in between these tests. To address the clinical consequences of mild tubal pathology, patients with mild tubal pathology should then be randomized to compare natural conception with IUI and IVF. Until such a trial has been conducted, the recommendations regarding expectant management versus treatment, in case of unilateral pathology, depends on several factors such as age of the woman and duration of subfertility. In patients with unexplained subfertility, the prognostic model by Hunault et al. (2004) following tubal testing is advised. The most important prognostic factors are age of the woman, duration of subfertility and whether or not the couple has ever had a pregnancy before consultation. If the chances for natural conception are above 30%, expectant management is generally recommended. Below 30%, treatment is advised (Steures et al., 2006).
References


Rekart ML, Brunham RC. Epidemiology of *chlamydial* infection: are we losing ground? *Sex Transm Infect* 2008; 84: 87-91.
Prognostic significance of HSG and laparoscopy


