Tubal subfertility and ectopic pregnancy. Evaluating the effectiveness of diagnostic tests

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Symptom-free women at increased risk for ectopic pregnancy: should we screen?

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Submitted

Abstract

Introduction: Transvaginal sonography, serum human chorionic gonadotrophin (hCG) measurement, and serum Progesterone measurement provide the possibility to screen symptom-free women at increased risk for ectopic pregnancy. Potential benefits of screening are the prevention of tubal rupture and the possibility of non-invasive treatment with systemic methotrexate, thereby reducing costs. Furthermore, it is not unlikely that women at increased risk for ectopic pregnancy want to be informed about the condition of their pregnancy as soon as possible.

Methods: A decision-analytic approach was used for the comparison of screening programs incorporating transvaginal sonography, serum hCG measurement, and serum Progesterone measurement with a 'watchful waiting' strategy. The strategies were compared on the expected number of prevented tubal ruptures, the expected number of false-positive diagnoses, and expected costs. Data were extracted from the literature.

Results: The number of false-positive diagnoses that were expected to be made to prevent one case of tubal rupture appeared to be strongly dependent on the prevalence of ectopic pregnancy, as were the expected costs to prevent one tubal rupture. Screening incorporating serum Progesterone measurement was less costly in case the prevalence for ectopic pregnancy was < 5%, but the number of false-positives and the costs per prevented tubal rupture were higher than after screening with transvaginal sonography and serum hCG measurement only. At a prevalence of ectopic pregnancy of 6%, a screening program with transvaginal sonography and serum hCG measurement would reduce the number of patients with ruptured ectopic pregnancy from 2.1 to 0.61 per 100 screened women. Screening was expected to cost approximately US$ 1,200 per prevented tubal rupture, whereas the number of expected false positive diagnoses was 0.64 per prevented tubal rupture.

Conclusion: Screening for ectopic pregnancy could reduce the number of patients with tubal rupture, but only at expense of a large false-positive rate. Although sonography in symptom-free women at risk for ectopic pregnancy might be justified for psychological reasons, the medical and economic benefits seem to be limited.
16.1 Introduction

The combination of transvaginal sonography and serum human chorionic gonadotrophin (hCG) measurement has shown excellent sensitivity and specificity in the diagnosis of ectopic pregnancy. It's use in the diagnosis of ectopic pregnancy in patients with clinical symptoms is therefore generally accepted. Some authors have advocated to apply these diagnostic tools - with or without performance of single serum Progesterone measurement - in symptom-free women at increased risk for ectopic pregnancy as well, since there is clear evidence that a history of tubal disease increases the risk of ectopic nidation of a new pregnancy.

If a screening approach is followed, women at increased risk for ectopic pregnancy are instructed to contact a gynecologist as soon as they think they are pregnant. When pregnancy is confirmed by a urine test, further testing can be done with transvaginal sonography, serum hCG measurement and serum Progesterone measurement or a combination of these tools. An alternative for a screening program for women at increased risk might be to advise them to contact the clinic as soon as clinical symptoms, i.e., abdominal pain and/or vaginal bleeding, occur.

An advantage of the early detection of ectopic pregnancy is that it usually allows intervention before tubal integrity is lost and before the patient’s condition has deteriorated, thereby preventing complications and improving clinical outcome. On the other hand, screening symptom-free women might induce false-positive diagnoses that lead to performance of laparoscopy or medical treatment in women without an ectopic pregnancy.

A formal analysis of the harms and benefits of screening for ectopic pregnancy has never been made. The aim of the present study was therefore to compare screening programs for ectopic pregnancy in symptom-free women with a strategy in which women are instructed to contact their gynecologist only when clinical symptoms occur. These strategies are compared with respect to prevention of tubal rupture, number of false-positive diagnoses, and costs by means of a decision-analytic model incorporating data from the literature.

16.2 Material and methods

A decision tree was constructed to compare two screening programs in which women at increased risk are instructed to contact a gynecologist as soon as they think they are pregnant, with a ‘watchful waiting’ strategy, in which pregnant women at increased risk are advised to contact their gynecologist when clinical symptoms occur (Figure 1). The decision-analysis was performed with SAS® software.

The first screening program used transvaginal sonography and, in case transvaginal sonography was inconclusive, serum hCG measurement. The tests are integrated in an algorithm that established or rejected the diagnosis ectopic pregnancy in a probabilistic way, as was described in chapter 12. The diagnosis ectopic pregnancy was made as soon as the probability for ectopic pregnancy after sonography exceeded 95%, whereas the diagnosis ectopic pregnancy was rejected if this probability fell below 1%. When the diagnosis remains uncertain after transvaginal sonography, i.e., between 1% and 95%, se-
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Table 1: Diagnostic performance and costs of various tests used in the decision analysis

<table>
<thead>
<tr>
<th>Variable (ref)</th>
<th>Likelihood Ratios</th>
<th>Costs (US$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum progesterone measurement $^8$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$&lt; 5$, $5-10$, $10-15$, $15-20$, $&gt; 20$</td>
<td>1.2, 4.7, 0.8, 0.39, 0.25</td>
<td>10</td>
</tr>
<tr>
<td>Initial TVS $^9$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intra-uterine gestational sac present/absent</td>
<td>0.07, 2.2</td>
<td>46</td>
</tr>
<tr>
<td>Ectopic cardiac activity/gestational sac</td>
<td>$\infty$</td>
<td></td>
</tr>
<tr>
<td>Ectopic mass, fluid or both</td>
<td>3.6, 4.4, 9.9</td>
<td></td>
</tr>
<tr>
<td>No adnexal pathology</td>
<td>0.55</td>
<td></td>
</tr>
<tr>
<td>Serum hCG with adnexal pathology at initial TVS $^9$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$&lt; 1,000$, $1,000 - 1,500$, $1,500 - 6,000$, $&gt; 6,000$</td>
<td>0.29, 0.79, 11, $\infty$</td>
<td>26</td>
</tr>
<tr>
<td>Serum hCG without adnexal pathology at initial TVS $^9$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$&lt; 1,000$, $1,000 - 1,500$, $1,500 - 2,000$, $2,000 - 6,000$, $&gt; 6,000$</td>
<td>0.62, 0.31, 0.63, 15, $\infty$</td>
<td>26</td>
</tr>
<tr>
<td>Serum hCG course after 2 days $^9$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decrease $&gt; 50%$, decrease $&lt; 50%$, any rise</td>
<td>0, 0.8, 3.3</td>
<td>26</td>
</tr>
<tr>
<td>Serum hCG course after 4 days $^9$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decrease $&gt; 50%$, decrease $&lt; 50%$, any rise</td>
<td>0.12, 1.5, 12</td>
<td></td>
</tr>
<tr>
<td>Diagnostic laparoscopy $^{11}$</td>
<td></td>
<td>Perfect test</td>
</tr>
<tr>
<td>Treatment with systemic MTX $^{11}$</td>
<td></td>
<td>1,000</td>
</tr>
<tr>
<td>Treatment with laparoscopic salpingostomy $^{11}$</td>
<td></td>
<td>1,500</td>
</tr>
<tr>
<td>False-positive diagnosis</td>
<td></td>
<td>2,500</td>
</tr>
</tbody>
</table>

TVS = Transvaginal sonography; hCG = human chorionic gonadotrophin in IU/L; MTX = Methotrexate.
### Table 2: Results of the analysis

<table>
<thead>
<tr>
<th>No. of EPs per 100 women</th>
<th>Expected number of tubal ruptures per 100 women</th>
<th>Expected number of false-positive diagnosis per 100 women</th>
<th>Expected total costs per 100 women (US $1,000)</th>
<th>Expected additional false-positive diagnoses per prevented tubal rupture (US $1,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Watchful waiting</strong></td>
<td><strong>Screening (TVS &amp; hCG)</strong></td>
<td><strong>Screening (P, TVS, &amp; hCG)</strong></td>
<td><strong>Watchful waiting</strong></td>
<td><strong>Screening (TVS &amp; hCG)</strong></td>
</tr>
<tr>
<td>1</td>
<td>0.36</td>
<td>0.41</td>
<td>0.44</td>
<td>0.12</td>
</tr>
<tr>
<td>2</td>
<td>0.73</td>
<td>0.50</td>
<td>0.69</td>
<td>0.13</td>
</tr>
<tr>
<td>3</td>
<td>1.1</td>
<td>0.75</td>
<td>0.90</td>
<td>0.13</td>
</tr>
<tr>
<td>4</td>
<td>1.5</td>
<td>0.53</td>
<td>0.89</td>
<td>0.13</td>
</tr>
<tr>
<td>5</td>
<td>1.7</td>
<td>0.51</td>
<td>1.0</td>
<td>0.18</td>
</tr>
<tr>
<td>6</td>
<td>2.1</td>
<td>0.61</td>
<td>1.2</td>
<td>0.17</td>
</tr>
<tr>
<td>7</td>
<td>2.4</td>
<td>0.68</td>
<td>1.4</td>
<td>0.17</td>
</tr>
<tr>
<td>8</td>
<td>2.8</td>
<td>0.77</td>
<td>1.6</td>
<td>0.17</td>
</tr>
<tr>
<td>9</td>
<td>3.1</td>
<td>0.84</td>
<td>1.7</td>
<td>0.18</td>
</tr>
<tr>
<td>10</td>
<td>3.5</td>
<td>0.92</td>
<td>1.9</td>
<td>0.17</td>
</tr>
<tr>
<td>15</td>
<td>5.2</td>
<td>1.1</td>
<td>2.6</td>
<td>0.18</td>
</tr>
<tr>
<td>20</td>
<td>6.8</td>
<td>1.3</td>
<td>3.4</td>
<td>0.21</td>
</tr>
<tr>
<td>25</td>
<td>8.4</td>
<td>1.5</td>
<td>4.0</td>
<td>0.25</td>
</tr>
<tr>
<td>30</td>
<td>10.0</td>
<td>1.6</td>
<td>4.7</td>
<td>0.24</td>
</tr>
</tbody>
</table>

* Since at a certain prevalence of ectopic pregnancy, screening becomes less costly compared to the 'Watchful waiting' strategy, cost-effectiveness ratios can not be calculated. At these prevalences screening becomes dominant over the 'watchful waiting' strategy.

TVS = Transvaginal sonography; P = serum Progesterone measurement.
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Ectopic pregnancy was diagnosed in case the serum hCG concentrations were rising and rejected in case the serum hCG concentrations were declining.

In the second screening program, single serum Progesterone measurement was performed before transvaginal sonography. Again, if the probability of ectopic pregnancy was < 1%, the diagnosis was rejected and no further testing was performed. If the probability for ectopic pregnancy after serum Progesterone measurement was ≥ 1%, further testing with transvaginal sonography, and if necessary, serum hCG measurement or repeat diagnosis was performed, as in the first screening program.

In the ‘watchful waiting’ policy, women at increased risk for ectopic pregnancy were instructed to contact their gynecologist only when clinical symptoms occur (Figure 1). An ectopic pregnancy could subsequently be diagnosed according to the diagnostic algorithm incorporating transvaginal sonography and serum hCG measurement or, alternatively, it may turn out that the clinical symptoms were not caused by an ectopic pregnancy.

Data

Data on the performance of transvaginal sonography and serum hCG measurement and on the performance of single serum Progesterone measurement were obtained from previous studies (Table 1). Furthermore, we made several assumptions; (1) tubal rupture was supposed to be absent when ectopic pregnancy is diagnosed in symptom-free women, (2) the prevalence of active bleeding of the tube and/or tubal rupture was supposed to be 30% when clinical symptoms are present, (3) tubal rupture was supposed to occur when an ectopic pregnancy was not diagnosed in the initial diagnostic process, be it in the ‘watchful waiting’ strategy or in one of the screening programs, and (4) 10% of patients without ectopic pregnancy undergoing the ‘watchful waiting’ strategy was supposed to have clinical symptoms.

The direct medical costs of transvaginal sonography, serum hCG measurement, and serum Progesterone measurement were calculated from administrative data in the Academic Medical Center. These costs included costs for staff, materials, equipment, housing, depreciation, and overhead, the latter both at a department level and a hospital level. Costs were calculated as Dutch guilders, and then converted to US Dollars (exchange rate US$1 = hfl 1.71). For the calculation of costs of treatment, a distinction was made between treatment of symptom-free women and treatment of women with clinical symptoms. Ectopic pregnancy in symptom-free women was supposed to be curable with systemic methotrexate without confirmative laparoscopy, which was expected to cost approximately US$ 1,500 per patient. Ectopic pregnancy in women with clinical symptoms was supposed to be curable with laparoscopic surgery, which was expected to cost approximately US$ 2,500 per patient. The costs of a false-positive diagnosis were supposed to be $ 1,500 per patient, due to unnecessary treatment with methotrexate.

Analysis

For each strategy we calculated the expected number of patients with an ectopic pregnancy with tubal rupture at the moment of diagnosis, the expected probability of a false-positive diagnosis, and the expected costs. For the two screening programs, the expected number of false-positive diagnoses established to prevent one tubal rupture and the expected
total costs made to prevent one tubal rupture were calculated. The ‘watchful waiting’ strategy was considered to be the reference strategy. The prevalence of ectopic pregnancy was varied between 1 and 30 per 100 pregnancies.

**Sensitivity analysis**

We performed sensitivity analyses on four parameters: costs of transvaginal sonography (between US$ 50 and US$ 200), the probability of tubal rupture after initial false-negative diagnosis (between 30% and 100%), the probability of complaints in patients without ectopic pregnancy in the ‘watchful waiting’ policy (between 10% and 30%), and the probability of tubal rupture in patients with complaints (between 25% and 60%). The sensitivity analyses were performed in a two-way design, i.e., for each of the parameters we calculated the corresponding prevalence of ectopic pregnancy, at which the costs to prevent one tubal rupture were US$ 5,000 and the corresponding prevalence of ectopic pregnancy at which the cost of screening and the cost of ‘watchful waiting’ were equal.

16.3 Results

Table 2 shows the results of the decision analysis. Both screening programs were expected to reduce the number of tubal ruptures compared to the ‘watchful waiting’ strategy, except at a prevalence of ectopic pregnancy of 1%. The probability of a false-positive diagnosis increased with the prevalence of ectopic pregnancy, and was higher for both screening strategies, as compared to a ‘watchful waiting’ strategy. The expected number of false-positive diagnoses was slightly lower after screening with transvaginal sonography and serum hCG measurement only as compared to screening with transvaginal sonography, serum hCG measurement and serum Progesterone measurement. The total costs increased as the prevalence of ectopic pregnancies increased. For low prevalences the ‘watchful waiting’ strategy was expected to be less costly than screening. Screening became less costly at prevalences of ectopic pregnancy of 7.9% and 8.8%, for programs without and with serum Progesterone measurement, respectively.

Table 2 also shows the expected number of false-positive diagnoses and the expected costs that had to be made to prevent one tubal rupture. At a prevalence of 1% screening was inferior as compared to ‘watchful waiting’, since it was expected to generate more false-positive diagnoses, but did not reduce the probability of tubal rupture. The expected number of false-positive diagnoses per prevented tubal rupture decreased when the prevalence of ectopic pregnancy increased. At a prevalence of 1%, the screening program with transvaginal sonography and serum hCG measurement had a higher number of expected false-positive diagnoses per prevented tubal rupture as compared to screening with transvaginal sonography, serum hCG measurement and serum Progesterone measurement. When the number of ectopic pregnancies per 100 women was 5, the expected number of false-positives that were made to prevent one tubal rupture was 0.78 for screening based on transvaginal sonography and serum hCG measurement alone, and 0.96 for screening based on serum Progesterone measurement, transvaginal sonography, and serum hCG measurement. When the prevalence of ectopic pregnancy increased to 25%, the number of false-positive diagnoses that were expected to
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Screening with P, TVS and hCG

Screening with TVS and hCG

Costs of screening equal to 'watchful waiting'

Cost per prevented tubal rupture US$ 5,000

Costs of transvaginal sonography (US$)

Probability of tubal rupture after false negative diagnosis

Costs of screening equal to 'watchful waiting'

Cost per prevented tubal rupture US$ 5,000

Probability of complaints in patients without EP in 'watchful waiting' group

Probability of complaints in patient with complaints

Figure 2A-D: Results of the two-way sensitivity analyses. The upper to lines in each figure represent the combination of parameters at which costs of screening are equal to costs of 'watchful waiting'. The lower two lines represent the combination of parameters at which screening costs US$ 5,000 to prevent one tubal rupture. At each of the sensitivity-analyses the other parameters have values as assumed in the initial analysis.

(P = serum Progesterone measurement; TVS = Transvaginal sonography; hCG = serum hCG measurement)

be made to prevent one tubal rupture decreased to 0.25 and 0.35, respectively.

The expected costs for the prevention of one tubal rupture also decreased when the prevalence increased. When the expected number of ectopic pregnancies per 100 women was 5, the expected costs to prevent one tubal rupture were US$ 3,700 and US$ 2,300, respectively. The screening programs became dominant over a 'watchful waiting' strategy at prevalences of 8% and 9% for programs without and with serum Progesterone measurement, respectively.

Sensitivity analysis

Figure 2A-D shows the results of the sensitivity-analyses. Increase of the costs of transvaginal sonography had a negative impact on the cost-effectiveness of screening, both for strategies without and with serum Progesterone measurement. In case the cost of
transvaginal sonography were more then US$ 60, screening with serum Progesterone measurement would be less costly than screening without serum Progesterone measurement. Decrease of the probability of tubal rupture after a false-negative diagnosis had no impact on the prevalence of ectopic pregnancy at which cost of screening were equal to costs of ‘watchful waiting’, but it increased the prevalence of ectopic pregnancy at which screening was expected to cost US$ 5,000 to prevent one tubal rupture. Variation of the probability of tubal rupture after a false-negative diagnosis had more impact on the cost-effectiveness of a screening program incorporating serum Progesterone measurement as compared to a screening program with transvaginal sonography and serum hCG measurement only.

Increasing the probability of complaints in patients without ectopic pregnancy in the ‘watchful waiting’ strategy decreased the costs that had to be made to prevent one tubal rupture. Increasing the probability of tubal rupture in patients with complaints had little impact on the prevalence of ectopic pregnancy at which cost of screening were equal to costs of ‘watchful waiting’, but it decreased the prevalence of ectopic pregnancy at which the screening was expected to cost US$ 5,000 to prevent one tubal rupture.

16.4 Discussion

Our model showed that screening for ectopic pregnancy is expected to reduce the probability of tubal rupture as compared to watchful waiting. However, screening, be it with transvaginal sonography and serum hCG measurement alone or with transvaginal sonography, serum hCG measurement and serum Progesterone measurement, was expected to increase the number of patients in whom the diagnosis ectopic pregnancy was made incorrectly. In a population of women with a prevalence of ectopic pregnancy of 5%, screening with transvaginal sonography and serum hCG measurement alone was expected to generate 0.78 false-positive diagnosis for each prevented tubal rupture, whereas for screening with serum Progesterone measurement this number was 0.96. From an economic point of view, screening was expected to reduce costs compared to watchful waiting at prevalences of 7.9% and 8.8% for screening without and screening with serum Progesterone measurement, respectively.

We used decision analysis to compare two screening programs with ‘watchful waiting’. From a methodological perspective, the best standard available to compare these strategies would be to perform a randomized clinical trial. However, such a trial would require enormous costs and effort. The decision analysis that we performed is an acceptable alternative for such a trial, although it has several limitations. First, we presumed perfect compliance of the women at increased risk. It is more realistic to assume that some women who are offered screening will not contact their gynecologist in case of pregnancy. A second limitation is that some of the probabilities used in the analysis are unknown. For example, no data exist on the occurrence of clinical symptoms in pregnant women without an ectopic pregnancy. We presumed the probability of such symptoms in women without ectopic pregnancy to be 10%. Sensitivity analysis showed that variation of this variable between 5% and 30% had little impact on the outcome of our analysis. A third
limitation of the decision analytic approach is that mutual independence had to be presumed between serum Progesterone measurement and serum hCG measurement. Although both tests have been compared previously, all studies fail to appreciate that serum hCG measurement can only be interpreted in relation to findings at transvaginal sonography.12-16

However, despite this presumed mutual dependence we found screening with serum Progesterone measurement not superior to screening with transvaginal sonography and serum hCG measurement alone. Even when in the sensitivity analysis the costs of one transvaginal sonography were increased to US$ 200, screening with serum Progesterone measurement was only slightly more cost-effective than screening with transvaginal sonography and serum hCG measurement only. Based on this outcome we conclude that serum Progesterone measurement does not improve the performance of a screening program for ectopic pregnancy, despite the fact that it can detect pregnancy failure.5-7

With respect to the use of serum Progesterone measurement, some authors have proposed to perform dilatation and curettage in women with a serum Progesterone level below 5 ng/mL.16 If such an intervention was necessary in a majority of the patients with early pregnancy failure, dilatation and curettage should have been incorporated in our decision tree. However, recent randomized clinical trials have shown that expectant management is a successful policy in a majority of the patients with early pregnancy failure17-18, thereby making diagnostic dilatation and curettage in patients with suspected ectopic pregnancy and low serum Progesterone levels an expensive policy.

Surprisingly, the analysis showed that at a prevalence of 1% the number of tubal ruptures after screening, be it with or without serum Progesterone measurement, was higher than after ‘watchful waiting’. This is explained by the fact that, starting from this very low prevalence, the diagnosis ectopic pregnancy is rejected incorrectly in a considerable amount of patients. This incorrect reassurance caused in our analysis an increased number of tubal ruptures in these patients, since the assumed tubal rupture rate is higher in a women with a false-negative diagnosis than in a woman who contacts her gynecologist immediately after the onset of complaints.

Offering a screening program for ectopic pregnancy to women can be done for several reasons. First, early diagnosis might prevent tubal rupture, thereby improving short-term clinical outcome, as well as the preservation of the functional capacity of the tube for future fertility. Although randomized clinical trials comparing conservative and radical surgery are lacking, cohort studies have reported that fertility prospects are slightly better after salpingostomy as compared to salpingectomy, especially in presence of contralateral tubal pathology.19,20 Although the present analysis indicates that screening is expected to prevent tubal rupture, one must realize that the fertility prospects in patients with a history of tubal disease are already decreased, thereby limiting the potential gain for conservative treatment.

Second, early diagnosis might allow non-invasive treatment with systemic methotrexate, thereby reducing costs. Although systemic methotrexate is unlikely to have a strong beneficial effect on health related quality of life and fertility prospects, it might be less costly for patients with serum hCG concentrations < 3,000 IU/L in a scenario without
confirmative laparoscopy. To benefit from these potential advantage of early diagnosis, ectopic pregnancies that were diagnosed in the screening programs were supposed to be treated with systemic methotrexate in a completely non-invasive strategy, whereas in the 'watchful waiting' strategy more expensive surgical treatment was presumed. Despite this assumption, screening only reduced costs at a prevalence > 10%.

Third, it is very likely that women at increased risk for ectopic pregnancy wish to be informed about the condition of their pregnancy as soon as possible. Unfortunately, there are no data available on the psychological impact of both screening for ectopic pregnancy and the knowledge of being at risk for an ectopic pregnancy. In our personal clinical experience, patients are only relieved if they have seen the intra-uterine pregnancy themselves, whereas they are not satisfied with the sole result of biochemical tests. Thus, although in our opinion transvaginal sonography should be performed somewhere in the first trimester, the exact timing remains subject to debate.

Our analysis showed clearly that the expected benefits of offering screening to women at increased risk for ectopic pregnancy depend on the prevalence of ectopic pregnancy. We are aware of two studies reporting on the prevalence of ectopic pregnancy in symptom-free women at increased risk. Cacciatore et al. reported the prevalence of ectopic pregnancy in a screening program to be 24% in a Finnish cohort. A cohort study among symptom-free women at increased risk for ectopic pregnancy that was presented in chapter 15, revealed a prevalence of 5.6%. An explanation for the high detection rate in the Finnish study is that women at increased risk, in whom initial transvaginal sonography showed an intra-uterine pregnancy, were not included systematically, which might have inflated the detection rate. Taking into account that risk indicators increase the risk for ectopic pregnancy by a factor 10, that the baseline risk for ectopic pregnancy is around 1% and that a substantial part of the patients will notice the pregnancy only after the occurrence of clinical symptoms, the prevalence of ectopic pregnancy in symptom-free women at increased risk is more likely to be near 6% than near 24%.

If the prevalence were to be around 6%, screening for ectopic pregnancy is expected to reduce the number of patients with ruptured ectopic pregnancy from 2.1 to 0.61 per 100 screened women. At such a prevalence, screening with serum Progesterone measurement will generate less false-positive diagnoses and is as costly as screening without serum Progesterone measurement. However, since the number of tubal ruptures is lower after screening with transvaginal sonography and serum hCG measurement, the number of false-positive diagnoses and the costs made to prevent one tubal rupture are higher for screening with serum Progesterone measurement. In our opinion, 0.64 false-positive diagnoses and US$ 1,200 make the value of screening for ectopic pregnancy questionable.

One could also consider screening for ectopic pregnancy in women pregnant after been evaluated for subfertility. In the Canadian Infertility Treatment Evaluation Study (CITES) the prevalence of ectopic pregnancy was 3% in women without tubal pathology, but 16% in women with abnormalities on hysterosalpingography and/or laparoscopy (personal communication). Thus, the usefulness of screening women pregnant after subfertility without tubal pathology becomes questionable, since the cost of screening are over US$
20,000 to prevent one case of tubal rupture, and since for each prevented tubal rupture two patients will be diagnosed false-positively as having an ectopic pregnancy. However, screening at a prevalence of 15% was expected to reduce costs as compared to watchful waiting, and the number of false-positive diagnoses per prevented tubal rupture when screening is performed with transvaginal sonography and serum hCG measurement was 0.34. Thus, screening women with tubal pathology who can conceive after subfertility is justified taking into account these rates. When screening subfertile women for the presence of ectopic pregnancy, one should take into account that the diagnostic performance of serum hCG measurement is strongly reduced in pregnancies that occur through IVF-ET.24

In our analysis we assessed the value of screening by calculating the number of false-positive diagnoses and the costs that was expected to be made to prevent one tubal rupture. Although from these perspectives screening for ectopic pregnancy did not seem to be a very attractive option, one should also take into account that many women with a history of fertility problems want to be informed about the condition of their pregnancy. As a consequence, sonography will be performed often in this situation on psychological and emotional grounds. Our analysis showed that one should be very careful with making a diagnosis and starting treatment in these situations. The merit of such sonographies is not the early detection of ectopic pregnancy, but rather the early reassurance that nothing is wrong with a normal pregnancy.

16.5 References


