Ectopic pregnancy: let’s cut! Strict laparoscopic approach to 194 consecutive cases and review of literature on alternatives

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From March 1989 to December 1995, 194 cases of ectopic pregnancy were diagnosed in our centre and treated following a strict laparoscopic protocol. A total of 193 cases was treated surgically and only one case was treated medically, because general anaesthesia was contraindicated. Altogether, eight laparotomies (4.1%) had to be performed; three primary and five secondary, due to uncontrollable haemorrhage \( n = 3 \) and too large pregnancy size \( n = 2 \). Peri- or postoperative complications were encountered in 24 cases (12.4%). Residual disease occurred in 14 cases (7.2%), all after a technically successful operative laparoscopic procedure. These cases received adjuvant therapy, either systemic administration of methotrexate or a second intervention. The overall laparoscopic cure rate was 88.1% (171/194). Conclusive follow-up data could be obtained concerning 110 cases with an active desire for pregnancy. Overall conception rate was 77.3%, with an ongoing pregnancy rate of 81.2% and a recurrence rate of 10.6%. A critical overview of the available data on non-surgical approaches is made, while the reported results are evaluated according to published data. It is concluded that at this stage a surgical approach by means of operative laparoscopic surgery should remain the gold standard in treating ectopic pregnancies.

Key words: ectopic pregnancy/laparoscopy/surgical treatment

Introduction

Ectopic pregnancy is still a very common, and possibly increasing, problem among healthy young women (Goldner et al., 1993), with a prevalence of 0.95% in women aged 14–40 years (Coste et al., 1994). As with many topics, no uniform approach can be found in the literature. Two main schools can be distinguished, surgical and non-surgical, each further subdivided. Options vary from abstinence from active therapy, i.e. expectant management, to radical surgery via laparotomy.

We analysed our series of consecutive cases, in order to evaluate the success rates, failures, complications and short and long term outcome of our strict laparoscopic protocol. Do we perform good medical practice according to the available data from all possible approaches?

Materials and methods

A compilation was made of 194 consecutive cases of ectopic pregnancy, in 185 women, diagnosed and treated in our centre from March 1989 to November 1995, following a strict laparoscopic protocol: ectopic pregnancy equals laparoscopy.

Diagnosis was essentially clinical and based for the majority of cases on case history, clinical signs and symptoms and physical examination, coupled with human chorionic gonadotrophin (HCG) assessment, either in urine or in serum, and transvaginal ultrasound. In a minority of cases a diagnostic curettage was performed to exclude the presence of intrauterine trophoblastic tissue.

Surgical intervention was performed under general anaesthesia, on an in-patient basis, either by or under the direct supervision of a senior staff member of the Centre for Reproductive Medicine. Time of surgery was either at the moment of diagnosis, in case of emergency, or otherwise the next morning, as part of the routine operative programme.

Postoperative follow-up consisted of serial HCG assessment (twice weekly) until complete negativity (<5 IU/l).

In the case of medical adjuvant therapy, methotrexate was systemically administered i.m. at a dosage of 1 mg/kg body weight, on an out-patient basis, to be repeated after 48 h, if necessary, under citrovorum rescue and haematological monitoring.

Results

Patients

In all, 185 women presented a total of 194 consecutive ectopic pregnancies from March 1989 till December 1995. During this observation period five women had one repeat ectopic pregnancy, while two presented with two recurrences, the remaining 178 having a single ectopic pregnancy.

Mean maternal age at the moment of diagnosis was 31.3 years, ranging from 18.6 to 41.6 years. Mean parity was 0.7, ranging from zero to five. Nulliparity was observed in 110 cases, of which only 67 were primigravid. Mean gestation was 2.5, ranging from one to 12.

Case history revealed at least one eliciting factor in 83 cases (42.8%), as listed in Table I.

Conception occurred spontaneously in 119 cases, of which 17 should be categorized as failed contraception: intrauterine device (IUD) \( n = 13 \), previous tubal ligation \( n = 3 \) and oral contraceptive use \( n = 1 \). A total of 57 pregnancies occurred after in-vitro fertilization (IVF) and the remaining 18 after ovulation induction, with or without insemination.

Pregnancies

Mean duration of amenorrhoea was 7.3 weeks, ranging from 5.0 to 15.7 weeks.

Mean size of the ectopic pregnancy at laparoscopy was 30 mm, ranging from 10 to 150 mm.
Laparoscopic approach to ectopic pregnancy

Table I. Eliciting factors

<table>
<thead>
<tr>
<th>Factors</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous ectopic pregnancy</td>
<td>34</td>
</tr>
<tr>
<td>IVF on tubal indication</td>
<td>21</td>
</tr>
<tr>
<td>Planned IVF on tubal indication, but spontaneous conception</td>
<td>12</td>
</tr>
<tr>
<td>Tubal surgery (other than ectopic pregnancy or ligation reversal)</td>
<td>15</td>
</tr>
<tr>
<td>IUD use</td>
<td>13</td>
</tr>
<tr>
<td>History of ascending genital tract infection</td>
<td>11</td>
</tr>
<tr>
<td>Tubal factor, diagnosed at previous laparoscopy or hysterosalpingogram</td>
<td>11</td>
</tr>
<tr>
<td>Ligation reversal</td>
<td>5</td>
</tr>
</tbody>
</table>

IUD = intrauterine contraceptive device.

Table II. Laparoscopic findings. Size 30 mm (10–150)

<table>
<thead>
<tr>
<th>Implantation site</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampullary&lt;sup&gt;a&lt;/sup&gt;</td>
<td>130</td>
</tr>
<tr>
<td>Isthmic</td>
<td>38</td>
</tr>
<tr>
<td>Isthmo-ampullary</td>
<td>10</td>
</tr>
<tr>
<td>Fimbrial</td>
<td>5</td>
</tr>
<tr>
<td>Cornual</td>
<td>3</td>
</tr>
<tr>
<td>Ovarian</td>
<td>4</td>
</tr>
<tr>
<td>Abdominal (peritoneal)</td>
<td>3</td>
</tr>
<tr>
<td>Unknown&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1</td>
</tr>
<tr>
<td>Hemoperitoneum</td>
<td>84</td>
</tr>
<tr>
<td>Tubal abortion</td>
<td>30</td>
</tr>
<tr>
<td>Rupture</td>
<td>33</td>
</tr>
<tr>
<td>Normal contralateral tube</td>
<td>104</td>
</tr>
</tbody>
</table>

<sup>a</sup>Including one case where exact localization could only be obtained during a second intervention.
<sup>b</sup>Intrauterine implantation was excluded after curettage.

Localization was irrevocably established in 192 ectopics out of a total of 194, during 193 procedures, one case not having had a laparoscopy and another case being bilateral. Overall, 95.9% were tubal pregnancies with a trend for the right tube (105 cases or 54.1% versus 81 cases or 41.8% in the left tube). Details on the implantation sites are listed in Table II.

In five cases a heterotopic pregnancy was found; two of these went on to deliver a healthy child, while the other three almost immediately ended in a spontaneous abortion.

### Treatment

In three cases no laparoscopy was performed. One patient received medical treatment, general anaesthesia being contra-indicated, and in the other two cases a primary laparotomy was performed, due to haemodynamic instability and a history of extensive abdominal surgery.

A third ‘primary’ laparotomy was performed after diagnostic laparoscopy showed too poor visualization to allow operative laparoscopy due to massive haemoperitoneum.

In the remaining 190 cases (97.9%) an operative laparoscopy was undertaken. In five cases a secondary laparotomy had to be performed because of uncontrollable haemorrhage (n = 3) and technical unfeasibility due to large pregnancy size (n = 2), resulting in a 97.4% technical success rate for operative laparoscopy (185/190). Further details can be found in Table III.

### Complications

In total, 24 cases (12.4%) had peri- or postoperative complications. Four were haemodynamically unstable, of which two developed a respiratory distress syndrome. In two cases major haemorrhage occurred during laparoscopy, due to uncontrollable interstitial bleeding and an iatrogenic rupture of the external iliac artery. In one case a rather minor fimbrial haemorrhage led to a secondary laparotomy 2 h after (apparently successfully) terminating her laparoscopy. One patient had elevated body temperature for 40 h postoperatively, the nature of which remains unclear. In 23 cases a blood transfusion was given.

Residual disease occurred in 14 cases (overall 7.2%), all after a technically successful laparoscopy (14/185 = 7.6%).

A more detailed examination shows a residual disease rate of 1.0% after salpingectomy (179) versus 12.2% after salpingotomy (10/82). To be complete, residual disease was observed once after fimbrial aspiration and twice after peritoneal aspiration and lavage.

Adjuvant therapy consisted of either systemic methotrexate (n = 10), or a second intervention (n = 7). In three cases (30.0%), repeated methotrexate administration failed.

The overall success rate of operative laparoscopy in the case of ectopic pregnancy is 90.0% (171/190), while the success rate of the laparoscopic approach is still 88.1% (171/194). The overall surgical approach scores as high as 92.3% (179/194).

### Hospital stay

Overall postoperative hospital stay was 1.95 days, ranging from 1 to 9 days. When laparotomy was performed it rose to 7.00 days, ranging from 4 to 9 days, while when uncomplicated laparoscopy could be performed it fell to 1.59 days, ranging from 1 to 6 days.

### Subsequent pregnancy outcome

Conclusive data could be obtained about 153 cases, of which 38 had no desire for pregnancy and five more abandoned active fertility treatment immediately after their ectopic pregnancy, leaving 110 cases with an active desire for pregnancy. Overall, in 85 cases (77.3%) a new pregnancy occurred, of which 69 (81.2%) were intrauterine and evolutive (overall = 62.7%), seven miscarriages occurred and nine ectopic pregnancies (10.6%) needed treatment.

Conception was spontaneous in 44 cases (51.8%). In eight cases ovulation induction was performed, totalling 52 cases.

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Table III. Treatment

<table>
<thead>
<tr>
<th>Medical</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical</td>
<td>193</td>
</tr>
<tr>
<td>Laparotomy</td>
<td>8</td>
</tr>
<tr>
<td>Salpingectomy</td>
<td>95</td>
</tr>
<tr>
<td>Salpingotomy</td>
<td>82</td>
</tr>
<tr>
<td>Fimbrial aspiration</td>
<td>6</td>
</tr>
<tr>
<td>Peritoneal aspiration and lavage</td>
<td>4</td>
</tr>
<tr>
<td>Ovariolysis or partial ovariectomy</td>
<td>3</td>
</tr>
<tr>
<td>Hysterotomy</td>
<td>2</td>
</tr>
<tr>
<td>Contralateral tubal surgery</td>
<td>23</td>
</tr>
</tbody>
</table>
(61.2%) of proven normal tubal transport. The remaining 33 cases (38.8%) conceived after IVF treatment.

Discussion

A very large number of publications on the management of ectopic pregnancies can be found in the literature, ranging from case reports to randomized trials and from therapeutic abstinence, the so-called expectant management, to radical surgery. The first objective of any treatment should always concern the patient: solving the problem using a safe and easy procedure, while offering optimal short and long term outcome. The second objective should be universal applicability: treating all or as many patients as possible according to a single and simple protocol, but still allowing personal adaptation for each individual patient.

An overall success rate of 88.1%, meaning primary resolution with laparoscopy only in 172 cases out of a cohort of 194 unselected cases, is congruent with recent published series offering 88.0% (Aharoni et al., 1993) to 91.4% (Paulsson, 1992), where selection is not mentioned. If we consider the overall surgical approach, the cure rate is as high as 92.3%. A laparoscopic approach can be applied to 99.0% of all encountered ectopic pregnancies and is technically feasible in 95.9% of all cases or 96.9% of all attempts (185/191). In the non-surgical approaches, selection, if mentioned, reduces the number of cases suitable for the chosen therapy. A laparoscopic approach can be applied to 99.0% of all encountered ectopic pregnancies and is technically feasible in 95.9% of all cases or 96.9% of all attempts (185/191). In the non-surgical approaches, selection, if mentioned, reduces the number of cases suitable for the chosen therapy. In Table IV, a compilation is made of all recent series on expectant single or in repeated doses and regardless of the route of administration. Where patient selection is clearly mentioned. Here we find reports ranging from 9.6% (Fernandez et al., 1991) to 73.2% (Paulsson et al., 1995), with a calculated mean of 28.5%, or suitable for almost one in every three cases. In Table VI, we can find success rates of recently reported larger series (n > 20) on expectant management. These reported success rates are always obtained in cohorts of selected cases and vary from 47.7% (Shalev et al., 1995b) to 85.7% (Fernandez and Frydman, 1994), allowing us to calculate a mean value of 65.7% as overall success rate for expectant management. In Table VII, we can find similar figures on medical treatment with methotrexate, either in single or in repeated doses and regardless of the route of administration. Success rates vary from 56.0% (Fernandez et al., 1993) to 95.0% (Fernandez et al., 1995), with a calculated mean value of 74.4% for medical treatment. Overall cure rates can be calculated combining either Tables IV and VI for expected management or Tables V and VII for medical treatment with methotrexate. These calculated overall cure rates are as low as 10.2% for expectant management and 21.2% for medical treatment, assuming correct diagnosis in each reported case.
Table VIII. Proven intrauterine pregnancies in series of suspected ectopic pregnancy

<table>
<thead>
<tr>
<th>Article</th>
<th>Suspected EP</th>
<th>Proven intrauterine pregnancy</th>
<th>Presumed EP (by exclusion) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tinga et al. (1990)</td>
<td>20</td>
<td>11</td>
<td>9 (45.0)</td>
</tr>
<tr>
<td>Check et al. (1992)</td>
<td>29</td>
<td>5</td>
<td>24 (82.8)</td>
</tr>
<tr>
<td>Lurie et al. (1995)</td>
<td>26</td>
<td>3</td>
<td>23 (88.5)</td>
</tr>
<tr>
<td>Hahlin et al. (1995)</td>
<td>80</td>
<td>19</td>
<td>61 (76.2)</td>
</tr>
<tr>
<td>Total</td>
<td>155</td>
<td>38</td>
<td>117 (75.5)</td>
</tr>
</tbody>
</table>

EP = ectopic pregnancy.

Table IX. Laparoscopic confirmation of suspected ectopic pregnancy

<table>
<thead>
<tr>
<th>Article</th>
<th>Pool</th>
<th>Proven EP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kadar (1990)</td>
<td>99</td>
<td>32 (31.7)</td>
</tr>
<tr>
<td>Sadek and Schiotz (1995)</td>
<td>57</td>
<td>53 (93.0)</td>
</tr>
<tr>
<td>Shalev et al. (1995)</td>
<td>374</td>
<td>298 (79.7)</td>
</tr>
<tr>
<td>Total</td>
<td>530</td>
<td>383 (72.3)</td>
</tr>
</tbody>
</table>

EP = ectopic pregnancy.

The old idea that a positive HCG assessment coupled with an empty uterine cavity on (even transvaginal) ultrasound scan equals an ectopic pregnancy, is not always true (Tinga et al., 1990). Recent publications report an intrauterine pregnancy percentage of 11.5% (Lurie et al., 1994) to 55.0% (Russell and Rodgers, 1991) in cohorts of early ‘presumed’ ectopic pregnancies. More details are given in Table VIII, where recently published series of these early ‘presumed’ ectopic pregnancies are listed. Adding them all up, one can calculate a mean value of 24.5% intrauterine pregnancies, ongoing or not, in these series of early pregnancies, clinically suspected to beectopics, a finding that may be due to oversensitive HCG assays. Similar data are reported in laparoscopy studies giving 31.7% (Kadar, 1990) to 93.0% (Sadek and Schiotz, 1995) laparoscopic confirmation in cohorts of suspected ectopic pregnancies. These data are listed in Table IX. Here one can calculate a mean confirmation value of 72.3%, giving an overdiagnosis in 27.7% in series of clinically suspected ectopic pregnancies. Focusing on (very) early pregnancy, Ankum et al. proposed the term of trophoblast in regression, describing those foggy cases of unknown implantation site, making up to 54% of all cases (Ankum et al., 1995).

Assuming a 25% overdiagnosis level, meaning a 1 in 4 ratio of cases not needing any treatment and thus responding to any possible treatment, one can now recalculate all above mentioned rates and ratios. Population selection decreases to 12.2% for expectant management (eliminating 25% on a total of 304 means eliminating 76 cases leaving 228 cases out of a recalculated total of 1867, or 1943 minus the same 76) and 24.5% for medical treatment (here a similar recalculation is made, except for the series reported by Paulsson et al., where clinical diagnosis was laparoscopically confirmed; thus, 67 cases or 25% of 267 have been eliminated, leaving 293 out of a new total of 1194). Success rates decrease to 56.6% for expectant management (no recalculation is made for the series reported by Fernandez and Frydman and Shalev et al. due to laparoscopic confirmation; thus 121 cases or 25% of 485 have been eliminated, resulting in a success series of 260 out of a new total of 459) and 65.8% for methotrexate treatment (eliminating 176 cases or 25% of 703, results in a success series of 347 out of a total of 527), resulting in overall cure rates of 6.9% for expectant management (12.2 of 56.6%) and 16.1% for medical treatment (24.5 of 65.8%). This figure does correspond to the reported overall cure rate of 9.4% for expectant management in a series of laparoscopically confirmed ectopic pregnancies (Shalev et al., 1995b).

The last column of Table VII lists recent series of repeated methotrexate administration, with a cumulative mean success rate of 85.2% (358/420). Thus, the calculated overall failure rate for medical treatment, after strict patient selection and repeat administration of methotrexate, is 14.8%. This means that one in every seven cases will ultimately undergo (rescue) surgical treatment, possibly in an emergency setting, leading to more radical surgery and higher complication rates (Martin Vivaldi et al., 1995); worrying figures if the initial objective is to avoid invasive and/or surgical therapies, possibly on an out-patient basis.

On top of all these data, there is one prospective, randomized trial comparing medical treatment (intratubal instillation of methotrexate in a single dose) and surgical treatment (salpingotomy), both laparoscopically, following the same diagnostic algorithm and selection protocol. Reported success rates highly favour the surgical approach, 92.7% (51/55) versus 61.4% (27/44), and the authors conclude that there is only a limited role for intratubal methotrexate in the treatment of ectopic pregnancy (Shalev et al., 1995a).

On the other hand, one must always bear in mind that an ectopic pregnancy is still a possibly life threatening situation: 30 cases of maternal death due to ectopic pregnancy were reported in the USA in 1987 (Centers for Disease Control, 1990), and that one is dealing with otherwise healthy and (relatively) young women.

Our series report a failure rate, necessitating adjuvant therapy, of 7.2%, fitting with literature data of 6.2% (Chapron et al., 1991) or 6.5% (Barnhart et al., 1994). Most failures occur after conservative treatment, which corresponds to a reported percentage of 2% after salpingectomy (Maymon et al., 1995). A failure rate of 12.2% after salpingotomy is slightly higher than the expected 6–8% (Rullin, 1995) or 7% (Maymon et al., 1995) reported in recent overviews, but still very acceptable compared to 15.5% (Seifer et al., 1993) or 18.0% (Popp et al., 1994) reported in other recent series.

Possible failure of treatment dictates that (strict) follow-up is mandatory, i.e. until full negativity of HCG concentrations is noted. HCG decline after non-surgical treatment of ectopic pregnancy is significantly longer than after surgical treatment (Stovall and Ling, 1993; Fernandez et al., 1995) and significantly longer after expectant management than after active medical treatment (Korhonen et al., 1994). It is important to know that during this prolonged follow-up period after nonsurgical treatment, rupture of haematosalpinx may always occur (Tulandi et al., 1992), even with declining HCG levels (Lurie et al., 1994b); with an overall reported incidence of 11.6% (Shalev et al., 1995b) to 19.2% (Lurie et al., 1994a),

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probably due to a marked increase in size and vascularity (Atri et al., 1992), which may even occur as part of the normal resolution process (Atri et al., 1993). These facts may imply a closer follow-up including repeated clinical re-evaluations with serial transvaginal ultrasounds, bearing in mind the presence of possibly active trophoblast. On top of that, our 30% failure rate for methotrexate as adjuvant therapy for residual disease, i.e. proven active trophoblast, supports our disbelief in medical treatment as the first line approach for ectopic pregnancy.

Another frequently encountered argument supporting the non-surgical approach is the possible financial benefit. Avoiding surgical procedures and/or hospital stay may lead to a theoretical money saving regime (Creinin and Washington, 1993), but an ambulatory treatment implying prolonged and closer follow-up, including repeated serum assays and transvaginal scans, amounts to a cost regime practically equal to that for in-patient surgery (Lecuru et al., 1995a).

A final argument favouring the surgical approach is pelvic assessment, leading to an accurate diagnosis in 99.0% (192/194) and to adapted on-the-spot treatment, including surgery on the contralateral side in 23 cases in our series. Some authors try to compensate for this lack of data by performing post treatment hysterosalpingography, failing to mention that (normal) patency does not guarantee normal fertility outcome or exclude recurrence (Lecuru et al., 1995b).

Conclusive data can be found concerning fertility outcome and recurrence in large series after non-surgical approach. Our series shows a conception rate of 77.3%, with an ongoing (intrauterine) pregnancy rate of 81.2% and a recurrence rate of 10.6%, comparable to previous reports of 67% pregnancy rate and 12% recurrence (Pouly et al., 1991).

Further data are necessary to evaluate the true value of the non-surgical approach in cases of ectopic pregnancy, but at this stage, we can find no conclusive arguments to recommend this approach. On the contrary, we feel that a surgical approach by means of the laparoscope should remain the gold standard and should be optimized further.

Concluding, we state that our data, supported by a critical overview of the available literature on all possible approaches, show that only the surgical approach, by means of operative laparoscopy, remains the gold standard of time.

References


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