1 INTRODUCTION

Recent advances in ultrasonographic technology enable detailed studies and evaluation of the rapidly developing embryo in vivo. It is at present the most accurate and reliable method for the evaluation of first trimester pregnancies and their complications. However, the precise role of ultrasound in the first trimester is still in evolution, mainly because of rapid development and availability of newer generations of ultrasonographic equipment, which enables better and earlier visualization of embryonic structures.

The correct use and interpretation of first trimester ultrasound examination requires a good understanding of normal early embryonic developmental milestones and ultrasonographic landmarks.

2 AIMS

Part I of this guideline examines the use of ultrasound examination in the management of women with pregnancy complications in the first trimester, and the basic requirements of such an examination. The role of routine first trimester ultrasound examination and the safety of such examination will be examined in Part II of this guideline.

3 INDICATIONS

An ultrasound examination may provide valuable information to assist patient management in, but not limited to, the following clinical conditions in the first trimester of pregnancy:

3.1 Confirmation of the presence of normal intrauterine pregnancy
3.2 Estimation of gestational age
3.3 Confirmation of embryonic life or early pregnancy failure
3.4 Evaluation of the cause of vaginal bleeding
3.5 Evaluation of suspected ectopic pregnancy
3.6 Confirmation of multiple pregnancy
3.7 Evaluation of suspected pelvic, ovarian or uterine pathology.

4 NORMAL ULTRASONOGRAPHIC EMBRYONIC DEVELOPMENTAL MILESTONES

Table 1 shows some important ultrasonographic milestones during early pregnancy.

The earliest detectable ultrasonographic evidence of pregnancy is thickening of the decidua at approximately 3 to 4 weeks of menstrual age. This sign, however, is nonspecific and therefore carries no significant value for clinical management of early pregnancy complications.
Table 1. Important transvaginal ultrasonographic milestones

<table>
<thead>
<tr>
<th>Gestational age (Menstrual day)</th>
<th>Crown-rump length (mm)</th>
<th>Signs</th>
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<tbody>
<tr>
<td>3 to 4 week</td>
<td>-</td>
<td>Thickening of endometrium and decidua</td>
</tr>
<tr>
<td>4 to 5 week</td>
<td>-</td>
<td>First appearance of gestational sac</td>
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<tr>
<td>5 week</td>
<td>1-2</td>
<td>First appearance of yolk sac and embryonic pole</td>
</tr>
<tr>
<td>5 to 6 week</td>
<td>5</td>
<td>Embryonic cardiac activity</td>
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By about 4.5 week, a small 2-3 mm gestational sac, which represents the chorionic cavity, can be visualized by transvaginal sonography (TVS). This is the first reliable sonographic evidence of pregnancy. The gestational sac does not lie within the endometrial space but is intradecidual, and is sonographically surrounded by an echogenic ring of trophoblastic and decidual reaction. These features assist the differentiation between a small true gestation sac from collection of blood or fluid within the uterine cavity, although such distinction could sometimes be difficult.

Visualization of the yolk sac/embryo complex is diagnostic of an intrauterine pregnancy and excludes blighted ovum. The yolk sac should always be seen with TVS when the gestational sac reaches a mean diameter of 8 mm at 5 to 6 week. With TVS, embryos as small as 1 to 2 mm may be identified at similar stage of pregnancy. Although embryonic cardiac activity may be demonstrable in some pregnancies as early as 35 days after onset of last menstrual period, or in embryos as small as 1 mm, the absence of cardiac activity at such early stage could be normal. Embryonic activity, however, should always be observed by TVS when the crown-rump length (CRL) is 5 mm or more.

It is important to realize that these milestones represent the average development of a normal pregnancy. The ability to demonstrate these sonographic milestones is not only affected by biological variations between individuals but also the quality of the ultrasound scanner, the frequency of the transducer, and the experience of the operator. In general, the same milestone is expected to be visualized 1 week later if transabdominal ultrasonography (TAS) is used (Table 2). In case of uncertainty, one should always act on the safe side and request a repeat examination later.

Table 2. Average time of detection of Various Parameters in Early Pregnancy by Ultrasonography (Menstrual day)

<table>
<thead>
<tr>
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<th>Transabdominal</th>
<th>Transvaginal</th>
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<tbody>
<tr>
<td>Gestational sac</td>
<td>Day 35-37 (5 mm φ)</td>
<td>Day 29-31 (2 mm φ)</td>
</tr>
<tr>
<td>Yolk sac</td>
<td>Day 42-45</td>
<td>Day 35-37</td>
</tr>
<tr>
<td>Embryo</td>
<td>Day 45 - 46 (~ 5 mm)</td>
<td>Day 35-40 (~ 2 mm)</td>
</tr>
<tr>
<td>Heart motion</td>
<td>Day 42 - 45</td>
<td>Day 35 - 37</td>
</tr>
</tbody>
</table>
5 EARLY INTRA-UTERINE DEMISE

For diagnostic purpose, the most important question is beyond what point, i.e. the discriminatory level, the absence of yolk sac or fetal cardiac activity can be considered definite signs of early pregnancy failure.

Using TVS, visualization of a discrete embryo >5 mm without fetal cardiac activity can be considered diagnostic of embryonic demise. If the embryo is less than 5mm, the absence of cardiac activity could be normal and a repeat sonogram should be performed at least 1 week apart. If only TAS is performed, the discriminatory level should be at least 9 mm.

In the absence of an embryonic pole, the major sonographic diagnostic criterion of early pregnancy failure is a large gestational sac without a yolk sac (i.e. a condition also called blighted ovum or anembryonic pregnancy). Using TAS, an mean sac diameter (MSD) < 20mm without a yolk sac is generally considered as diagnostic of blighted ovum. With TVS under research setting, a much smaller discriminatory level of MSD of 8mm was proposed. However, more recent review of medical records in real clinic practices suggested that pregnancy failure should not be diagnosed based on the absence of yolk sac alone unless the MSD is 16mm or more. This higher discriminatory level was probably a result of variations in the quality of ultrasound machines and experience of operators. To avoid over-estimation of pregnancy failure, the Hong Kong College recommends that a diagnosis of a “blighted ovum” should only be made when the mean sac diameter is greater than 20 mm in the absence of an embryo or yolk sac.

In summary, when the mean gestational sac diameter is less than 20 mm or the crown rump length is less than 5 mm, an examination should be repeated at least one week later to determine the presence of fetal heart activity as well as growth of the gestational sac.

6 DIAGNOSIS OF EXTRAUTERINE PREGNANCY

Major ultrasonographic features of extrauterine pregnancy (EUP) include the presence of a gestational sac in the fallopian tube containing a viable embryo, an adnexal ring and a complex adnexal mass, or the absence of an intrauterine pregnancy (IUP).

Before the era of transvaginal ultrasonography, diagnosis of an extrauterine pregnancy was mainly made by exclusion. An adnexal mass may be detected by the transabdominal approach in between 35 and 50% of women with ectopic pregnancy.

Using TVS, adnexal abnormalities are present in 95% of symptomatic EUP. A gestational sac with viable embryo in the fallopian tube is diagnostic of EUP, but is only seen in 11.9% of symptomatic subjects. The presence of a complex adnexal mass is the commonest ultrasonographic adnexal abnormality, which although is not diagnostic of an EUP has a high specificity of 98.9%.

Due to the increasing use of routine ultrasound examination in “normal” asymptomatic early pregnancies, the only ultrasonographic suspicion of EUP may be the failure to visualize an IUP. In normal circumstances, the presence of an intrauterine gestational sac suffices to preclude the possibility of an EUP because of the rare occurrence of heterotopic pregnancies. However, failure to visualize an IUP may be due to conditions other than ectopic pregnancy, and the commonest is early IUP. Under this circumstances, quantification of maternal serum hCG may be useful.

Kadar et al first introduced the concept of hCG discriminatory zone, which was defined as the minimal hCG concentration above which the sac of an IUP should always be identifiable using sonography. In clinical practice, the following issues concerning this discriminatory zone have to be carefully considered:
6.1 Different laboratories use different reference standards of hCG, including the 3rd International Standard (IS), formerly known as 1st International Reference Preparation (IRP), and the 2nd IS. The 3rd IS value is approximately twice the value yielded by the 2nd IS. One should always confirm with their laboratory which reference standards they are using.

6.2 With TAS, Kadar et al in 1981 suggested that the discriminatory zone was between 6,000 and 6,500 mIU/mL (1st IRP). Since then, TVS was introduced and resolution of sonography improved greatly. As a result, a much lower discriminatory zone as low as 1,000 mIU/mL was reported\textsuperscript{12}. Taken into account of differences in ultrasound scanner and experience of operators, the most commonly used discriminatory zone for TVS is 2,000 mIU/mL (3rd IS)\textsuperscript{13,14,15}. It is possible that this level may be further reduced in the future.

6.3 In generally, absence of IUP by TVS together with an hCG above the discriminatory zone is highly suggestive of EUP, and further diagnostic investigation is warranted. If TVS is non-diagnostic and hCG is below the discriminatory zone, quantification of hCG should be repeated every 2 days and TVS be repeated when hCG rises beyond the discriminatory zone\textsuperscript{13}.

6.4 Clinical management should also take into account of patient symptomatology because EUP may rupture even if the serum hCG is below the discriminatory zone\textsuperscript{16}.

6.7 The examination can be carried out either transabdominally or transvaginally. When one modality fails to provide sufficient information, the other modality should be performed to provide additional information.

8 THE EXAMINATION

8.1 The location of the gestational sac, and the presence or absence of an embryo and/or yolk sac should be documented.

8.2 The crown-rump length (CRL) or, if the embryonic pole is not visible, the size of gestational sac should be measured. Gestational assessment should preferably be based on CRL, which when measured between 8 and 12 weeks is the most accurate method for such purpose.

8.3 Comments on the characteristics of the gestational sac including the diameters (three dimensions in two perpendicular planes) of the sac space and the hyperechoeic rim should be made whenever this is useful to suggest abnormality. Similarly, abnormally large or small yolk sac sizes should be commented upon.

8.4 The presence or absence of fetal cardiac action should be reported.

8.5 The number of fetuses should be determined.

Multiple pregnancies should be reported as such only when multiple embryos/fetuses are identified. An attempt should be made to determine the presence or absence of intervening membrane(s) between the fetuses and to determine the chorionicity. A first trimester ultrasound examination has the advantage over a second trimester examination because of its higher accuracy in determining the chorionicity. This has important implications in counselling women who may need prenatal diagnosis.
In dichorionic twins, the insertion of the intervening membranes is lambda(λ)-shaped with placental tissue extending between the intervening membranes. This is known as the ‘twin-peak’ sign. This sign gradually disappears with advancing gestation and may or may not be observable after the second trimester. In monochorionic twins, the intervening membrane insertion is T-shaped. (NB This T-shape sign is not applicable in early gestation before the amnion fuses with the chorion. Prior to this, one can count the number of amniotic and chorionic cavity to decide amnionicity and chorionicity. It is only after the fusion of amnion and chorion when the “Twin Peak” sign become useful and necessary.)

8.6 Evaluation of the uterus (including the cervix) and the adnexal structures should be performed. During pregnancy, local myometrial contractions may mimic intramural leiomyomas on ultrasound examination. In case of doubt, repeating the ultrasound examination after 30 minutes or on another occasion will resolve the uncertainty.

9 DOCUMENTATION

Adequate documentation is essential for quality patient care. This should include a permanent record (that includes thermal paper images, Polaroid, X-ray films, computer or laser discs) of the following ultrasound images:

9.1 the gestational sac including the embryo (if present)

9.2 the CRL view of the fetus, and if measured, the BPD and the FL views

9.3 views of the adnexal or uterine abnormalities (if detected)

10 RECOMMENDATIONS

10.1 Ultrasound examination is essential in the management of early pregnancy complications and diagnosis of early pregnancy failure.

10.1.1 The diagnosis of early pregnancy failure is equivalent to the certification of death of a human being. Such diagnosis should never be made unless the sonographic signs are definite and unequivocal.

10.1.2 Whenever there is uncertainty, even the slightest doubt, the examination should be repeated at least 1 week later to monitor the growth of gestational sac or the appearance of fetal cardiac activity.

10.2 Documentation of the indication(s) and the findings of the ultrasound examination are essential.

REFERENCE LIST


ACKNOWLEDGEMENT:

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This guideline was produced by the Hong Kong College of Obstetricians and Gynaecologists as an educational aid and reference for obstetricians and gynaecologists practicing in Hong Kong. The guideline does not define a standard of care, nor is it intended to dictate an exclusive course of management. It presents recognized clinical methods and techniques for consideration by practitioners for incorporation into their practice. It is acknowledged that clinical management may vary and must always be responsive to the need of individual patients, resources, and limitations unique to the institution or type of practice. Particular attention is drawn to areas of clinical uncertainty where further research may be indicated.