Recurrent Pregnancy Loss

Guideline of European Society of Human Reproduction and Embryology

Update 2022

ESHRE Recurrent Pregnancy Loss Guideline Development Group

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INFERTILITTY FELLOWSHIP

A diagnosis of Recurrent Pregnancy Loss (RPL) could be considered after the loss of two or more pregnancies

There was some discrepancy in opinions among the guideline group members regarding the definition. Some guideline group members would like to stress that they disagree with the suggested definition and will keep a definition of three or more consecutive losses in their clinical practice

The GDG believes that defining RPL as two or more pregnancy losses will facilitate research, shared decision-making and psychological support to couples. In addition, testing for APS, a treatable subdiagnosis of RPL, can be performed after two losses

A pregnancy in the definition is confirmed at least by either serum or urine b-hCG, i.e. including nonvisualized pregnancy losses (biochemical pregnancy losses and/or resolved and treated pregnancies of unknown location)

In the non-visualized pregnancy loss group, pregnancy losses after gestational week 6 are included, where an ultrasound examination was only done after complete expulsion of the embryo and trophoblast, or no ultrasound was done after heavy bleeding: it includes pregnancies that would have been classified as clinical miscarriages in case an earlier ultrasound scan had been done.

ectopic and molar pregnancies should not be included in the definition.
Implantation failure is also excluded from the definition. Pregnancy losses both after spontaneous conception and after ART treatments should be included in the definition.

The GDG concludes to use the term Recurrent Pregnancy Loss.

We recommend the use of ‘recurrent pregnancy loss’ to describe repeated pregnancy demise and to reserve ‘recurrent miscarriage’ to describe cases where all pregnancy losses have been confirmed as intrauterine miscarriages.

The term therefore includes all pregnancy losses (PLs) from the **time of conception** until **24 weeks** of gestation.

PREVALENCE OF RPL

thus find that the RPL prevalence is between 0.8% and 1.4% among women with ≥2 pregnancies

Pregnancy loss is a significant negative life event and the repetitive nature of RPL may intensify the grief experienced. Studies have mostly focused on women, and there is a need for studies on the emotional impact of RPL on men.

Clinicians and clinics should take the psychosocial needs of couples faced with RPL into account when offering and organizing care for these couples.

More information on caring for the RPL couple is presented in PART B.

Risk factors for RPL

Female age

Women should be sensitively informed that the risk of pregnancy loss is lowest in women aged 20 to 35 years.	Strong	⊕⊕■■
Women should be sensitively informed that the risk of pregnancy loss rapidly increases after the age of 40.	Strong	⊕⊕■■

STRESS

Recommendation		
Stress is associated with RPL, but couples should be informed that there is no evidence that stress is a direct cause of pregnancy loss.	Strong	⊕■■■

OCCUPATIONAL OR ENVIRONMENTAL EXPOSURE

. In the first study serum zinc, copper, and vitamin E levels were significantly lower in 35 women with RPL and serum selenium, lead, and cadmium were significantly higher compared with 34 controls, which could indicate that heavy metals and a lack of micronutrients could cause pregnancy loss in women with RPL

In the second study, higher levels of organochlorine pesticides were detected in blood of 30 women with RPL compared to 30 controls, which could indicate an association between organochlorine pesticides and RPL

. Another study reported an increased risk of pregnancy loss in personnel exposed to **anaesthetic gases** in operating and recovery rooms as compared to non-exposed hospital staff

Based on only a few small studies, exposure to occupational and environmental factors (heavy metals, pesticide, lack of micronutrients) seems to be associated with an increased risk of pregnancy loss in women with RPL.

Although exposure to possible hazardous substances should be avoided during pregnancy (for all pregnant women), there are insufficient data to recommend protection against a certain occupational or environmental factor in women with RPL.

CHRONIC ENDOMETRITIS

Chronic endometritis is characterized by a plasma cell infiltrate in the endometrium associated with a range of pathogenic organisms.

Further research is needed including prospective observational studies and randomized controlled trials before screening women for endometritis can be recommened

ENDOMETRIAL DECIDUALIZATION AND SENESCENCE

Decidualization denotes differentiation of resident stromal cells into specialist decidual cells, which transform the endometrial mucosa into a robust, tolerogenic matrix to accommodate invading trophoblast

At present, however, biomarkers of senescent decidual cells have not been validated for clinical use.

SMOKING CESSATION

Recommendation	
Couples with RPL should be informed that smoking could have a negative impact on their chances of a live birth, and therefore cessation of smoking is recommended.	GPP

STRIVING FOR A HEALTHY, NORMAL RANGE BODY MASS INDEX

Recommendation		
Couples with RPL should be informed that maternal obesity or being significantly underweight is associated with obstetric complications and could have a negative impact on their chances of a live birth and on their general health.	Strong	⊕⊕■■
Striving for a healthy normal range BMI is recommended.	GPP	

CAFFEINE INTAKE

Some studies have also suggested caffeine intake as a risk factor for RPL, but not all studies reported an association. An association has been described between caffeine intake and **late pregnancy** loss.
Based on the evidence, it is **unclear** whether caffeine intake is a risk factor for RPL

EXERCISE

one large cohort study reported a graded association between exercise and higher risk of miscarriage, and two studies showed the same risk for miscarriage in exercising versus nonexercising pregnant women With regards to occupational physical activity,
three studies reported no effect, while two high-quality studies pointed to high-intensity occupational activity as a risk factor for miscarriage

AVOIDING ALCOHOL

Recommendation		
Couples with RPL should be informed that excessive alcohol consumption is a possible risk factor for pregnancy loss and proven risk factor for fetal problems (Fetal alcohol syndrome).	Strong	⊕⊕■■
Couples with RPL should be advised to limit alcohol consumption.	GPP	

OTHER LIFESTYLE CHANGES

Women with threatened early pregnancy loss are often advised to refrain from intercourse at least until the bleeding/pain have stopped, but this advice is based on presumptions of the doctor, not clinical evidence. Until evidence is available, clinicians are recommended to inform women asking about intercourse during pregnancy and pregnancy loss, that there is no evidence on the topic.

Similarly, we found no evidence that using soft drugs(e.g., cannabis) could be a risk factor for pregnancy loss in women with RPL .

However, avoiding soft drugs is in general recommended, and especially during pregnancy

GENETIC ANALYSIS OF PREGNANCY TISSUE FOLLOWING PREGNANCY LOSS

Recommendation

Genetic analysis of pregnancy tissue following pregnancy loss is not routinely recommended but it could be performed for explanatory purposes.	Conditional	⊕⊕■■
For genetic analysis of the pregnancy tissue following pregnancy loss, array-CGH is recommended based on a reduced maternal contamination effect.	Strong	⊕⊕■■

Justification

	Association	Contributing factor	Prognosis	Treatment
Karyotyping of the pregnancy tissue following pregnancy loss	Yes	Yes	No	No

PARENTAL GENETIC ANALYSIS

Recommendations

Parental karyotyping could be carried out after individual assessment of risk for diagnostic purposes.	Conditional	⊕⊕■■

Justification

	Association	Contributing factor	Prognosis	Treatment
Parental genetic testing	Yes	Yes[1]	Yes[2]	PGT, adoption, gamete donation or other alternatives

1 For couples with a parental chromosome abnormality, about one third of pregnancy losses are caused by

HEREDITARY THROMBOPHILIA

Recommendation

For women with RPL, we suggest not to screen for hereditary thrombophilia unless in the context of research, or in women with additional risk factors for thrombophilia.	Conditional	⊕⊕⊕■

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Justification

	Association	Contributing factor	Prognosis	Treatment
Hereditary thrombophilia*	No/weak	Unclear	Yes	No

**** This includes Factor V Leiden mutation – Prothrombin mutation – MTHFR mutation – Protein C, Protein S and Antithrombin deficiency***

ACQUIRED THROMBOPHILIA

Recommendations

For women with RPL, we recommend screening for antiphospholipid antibodies (LA and ACA [IgG and IgM]), after two pregnancy losses.	Strong	⊕⊕■■
For women with RPL, screening for aβ2GPI can be considered after two pregnancy losses.	GPP	

Justification

	Association	Contributing factor	Prognosis	Treatment
Antiphospholipid antibodies: LA and ACA (IgG and IgM)	Yes	Yes	Yes	Weak evidence
aβ2GPI	Possible (not statistically significant)	Possible	No data	No data

HUMAN LEUKOCYTE ANTIGEN

Recommendation (updated in 2022)

Human Leukocyte Antigen (HLA) determination in women with RPL is not recommended in clinical practice. Only HLA class II determination (HLA-DRB1*15:01, HLA-DRB1*07 and HLA-DQB1*05:01/05:02) could be considered in Scandinavian women with secondary RPL after the birth of a boy, for explanatory and prognostic purposes.	Conditional ⊕⊕■■

Justification

	Association	Contributing factor	Prognosis	Treatment
HLA-compatibility	Controversial evidence	NA	No prognostic potential	NA
HLA class II: HLA-DR and HLA-DQ (maternal)	Strong, but only shown in Scandinavian women	YES, especially for secondary RPL after first born boy	Negative impact on future live birth	None available
HLA-G	Significant but weak	No data	No data	NA
KIR and HLA-C	Controversial evidence	No data	No data	NA

ANTI-HY ANTIBODIES

Measurement of anti-HY antibodies in women with RPL is not recommended in clinical practice.	Conditional ⊕⊕■■

Justification

	Association	Contributing factor	Prognosis	Treatment
Anti-HY immunity	Moderate (Only shown in Scandinavian women)	YES, especially for secondary RPL after first born boy	Negative impact on future live birth*	None available

** Prognostic impact is stronger for women with secondary RPL with a first-born boy and HLA class II alleles*

CYTOKINES

Recommendations

Cytokine testing should not be used in women with RPL in clinical practice.	Strong	⊕⊕■■
Cytokine polymorphisms should not be tested in women with RPL.	Strong	⊕⊕⊕■

Justification

	Association	Contributing factor	Prognosis	Treatment
Cytokines	Yes	Unclear	Unknown	NA
Polymorphisms in cytokine genes	No association	NA	NA	NA

ANTINUCLEAR ANTIBODIES (ANA)

Recommendation

Antinuclear antibodies (ANA) testing could be considered for explanatory purposes.	Conditional ⊕⊕■■■

Justification

	Association	Contributing factor	Prognosis	Treatment
ANA antibodies	Yes	Probably not – no documentation	Unclear	NA

NATURAL KILLER CELLS (NK CELLS)

Recommendation

There is insufficient evidence to recommend NK cell testing of either peripheral blood or endometrial tissue in women with RPL.	Strong	⊕■■■

Justification

	Association	Contributing factor	Prognosis	Treatment
NK in Peripheral blood: numbers	Weak	No	Unclear – No	No
NK cell cytotoxicity in peripheral blood	Unclear	/	No	No
NK in endometrium / uterine	Weak	/	Unclear	No

From studies analysing NK cells in peripheral blood lymphocytes before or during pregnancy, there

Recommendation		
Testing anti-HLA antibodies in women with RPL is not recommended.	Strong	⊕⊕⊕■

Antisperm antibodies

Antisperm antibodies have also been described in women with RPL, although the results are inconsistent, and the relevance is unclear.

Celiac disease serum markers

transglutaminase (tTG) antibodies and endomysialantibodies (IgA + IgG)

is not indicated in women with RPL in absence of symptoms of celiac disease

THYROID DYSFUNCTION

Recommendations

Thyroid screening (TSH and TPO antibodies) is recommended in women with RPL.	Strong	⊕⊕⊕■
Abnormal TSH levels should be followed up by T4 testing in women with RPL.	Strong	⊕⊕⊕■

	Association	Contributing factor	Prognosis	Treatment
Hypothyroidism	Only sporadic PL	Only for sporadic PL	Yes	Supplementation of Levothyroxine
Subclinical hypothyroidism	Yes	Yes	No clear effect as of yet.	Unknown if effective
Hyperthyroidism	No	No	No clear effect as of yet.	Yes: Propylthiouracil
TPO-antibodies	Yes	Yes	Yes	Need for treatment studies
TG antibodies	No*	Mostly detected combined with TPO antibodies	Yes	Need for treatment studies

**** No association has been found based on the evidence included in this guideline.***

Based on a high prevalence of subclinical hypothyroidism and thyroid auto immunity in women with RPL and potential of treatment options, testing for thyroid function is recommended.

PCOS AND DISTURBANCES OF THE INSULIN METABOLISM

Assessment of PCOS, fasting insulin and fasting glucose is not recommended in women with RPL to improve next pregnancy prognosis.	Strong ⊕⊕■■

Justification

	Association	Contributing factor	Prognosis	Treatment
PCOS	YES	YES	NO	Metformin for sporadic PL no studies for RPL
Insulin resistance*	YES (OR 3.6)	Unclear	No studies	No studies
Fasting insulin	Inconsistent (2 YES, 1 NO)	Unclear	No studies	No studies
Fasting glucose	NO	NO	No studies	No studies

** IR calculated based on fasting insulin and fasting glucose*

HYPERPROLACTINEMIA

Recommendation

Prolactin testing is not recommended in women with RPL in the absence of clinical symptoms of hyperprolactinemia (oligo/amenorrhea).	Conditional	⊕⊕■■

Justification

	Association	Contributing factor	Prognosis	Treatment
Prolactin	Inconsistent results	No data	Possible	Yes

OVARIAN RESERVE TESTING

Recommendation

Ovarian reserve testing is not routinely recommended in women with RPL.	Strong	⊕⊕■■

Justification

	Association	Contributing factor	Prognosis	Treatment
Ovarian reserve	Unclear	Unclear	Abnormal CCCT = poor LBR	No studies

LUTEAL PHASE INSUFFICIENCY

Recommendation

Luteal phase insufficiency testing is not recommended in women with RPL.	Strong ⊕⊕■■

Justification

	Association	Contributing factor	Prognosis	Treatment
Luteal phase insufficiency testing*	Inconsistent	No data	No	possible

** Midluteal progesterone or endometrial biopsy*

ANDROGENS

Recommendation

Androgen testing is not recommended in women with RPL.	Strong	⊕⊕■■

Justification

	Association	Contributing factor	Prognosis	Treatment
Androgens (Testosterone)	Inconsistent (2 YES vs 1 NO)	/	No	/
Elevated FAI*	/	/	Possible	/

Free androgen index

VITAMIN D

	Association	Contributing factor	Prognosis	Treatment
Vitamin D	Possible	Possible	/	Vitamin D supplementation

LUTEINIZING HORMONE (LH)

Recommendation

LH testing is not routinely recommended in women with RPL	Strong	⊕■■■

Justification

HYPERHOMOCYSTEINEMIA

Recommendation

Measurement of homocysteine plasma levels is not routinely recommended in women with RPL.	Strong	⊕■■■

Justification

	Association	Contributing factor	Prognosis	Treatment
Hyperhomo-cysteinemia	Inconsistent	Possible in PCOS	No data	(High-dose) folic acid and vit B6 LMWH + aspirin

CONGENITAL UTERINE MALFORMATIONS

Recommendations (updated 2022)

All women with RPL should have an assessment of the uterine anatomy.	Strong	⊕⊕■■
The preferred technique to evaluate the uterus is transvaginal 3D US, which has a high sensitivity and specificity, and can distinguish between septate uterus and bicorporeal uterus (former AFS bicornuate uterus) with normal cervix.	Conditional	⊕⊕■■
Sonohysterography (SHG) is more accurate than HSG in diagnosing uterine malformations. It can be used to evaluate uterine morphology when 3D US is not available, or when tubal patency has to be investigated.	Conditional	⊕⊕■■

If a Müllerian uterine malformation is diagnosed, further investigations (including investigation of the kidneys and urinary tract) should be considered.	Conditional	⊕⊕■■
MRI is not recommended as first line option for the assessment of uterine malformations in women with RPL but can be used where 3D US is not available.	Conditional	⊕⊕■■
All women with RPL could have 2D ultrasound to rule out adenomyosis.	Conditional	⊕⊕■■

hysterosonography

uterine abnormalities than hysterosalpingography (HSG) or ultrasound (US) alone

higher sensitivity and specificity than HSG or diagnostic hysteroscopy to diagnose uterine malformations in genera

The diagnosis of septate uterus by SHG eliminates the need to perform laparoscopy prior to hysteroscopic metroplasty

Three-dimensional US

visualization of the internal and external contour of the uterus

high sensitivity and specificity, and it is non-invasive

may conveniently become the only mandatory step in the assessment of the uterine cavity in women with a history of RPL

2D transvaginal ultrasound (TV-US) and HSG

2D US has a low sensitivity, but a high specificity for diagnosis of malformations

HSG good sensitivity for diagnosing uterine malformations, but it is limited in differentiating between the types of malformations

Magnetic resonance imaging (MRI)

The accuracy and practicality of MRI has not yet been determined for the diagnosis of uterine malformations

helpful in the detecting renal malformations that are frequently associated with uterine malformations

higher costs and the absence of a diagnostic benefit compared to 3D US, MRI is not recommended as a first line option

Male factors

Recommendations (updated 2022)

In couples with RPL, it is recommended to assess lifestyle factors in the male partner (paternal age, smoking, alcohol consumption, exercise pattern, and body weight).	Strong	⊕⊕▪▪
Assessing sperm DNA fragmentation in couples with RPL could be considered for diagnostic purposes.	Conditional	⊕⊕⊕▪

Justification

	Association	Contributing factor	Prognosis	Treatment
Sperm DNA damage	Yes	Yes	requires further clarification	Changing lifestyle and for couples having ICSI, the use of hyaluronan selection looks promising. Further studies are needed to confirm this benefit.

Assessing prognosis of a couple with RPL

Reproductive history

Sex of firstborn

Family history

Recommendation (updated 2022)		
The GDG recommends to base prognosis on the woman's age and her complete pregnancy history, including number of previous pregnancy losses, live births, and their sequence.	Strong	⊕⊕⊕■
Prognostic tools (Kolte & Westergaard) can be used to provide an estimate of subsequent chance of live birth in couples with RPL.	GPP	

PREIMPLANTATION GENETIC TESTING (PGT) FOR UNEXPLAINED RPL

The second prospective study compared the outcomes of women with RPL and recurrent implantation failure (RIF) undergoing IVF. Women with RPL (n=41) undergoing PGT-A and women with RPL but no PGT-A (n=38) were compared with women with RIF undergoing PGT-A (n=42) or not (n=50)

PGT-A was shown to reduce the biochemical pregnancy loss and increase the live birth rate per embryo transfer in both groups

were no significant difference in the live birth rates per patient undergoing or not undergoing PGT-A (26.8% vs 21.1% in the RPL group and 35.7% vs 26.0% in the RIF group, respectively).

PREIMPLANTATION GENETIC TESTING FOR RPL WITH GENETIC BACKGROUND

Data on PGT-SR versus expectant management for couples with translocations reports a live birth rate of 37.8% on the first pregnancy after PGT-SR and 53.8% on the first natural pregnancy after ascertainment of the carrier status

. PGT-SR reduced the miscarriage rate, but cumulative live birth rate and time to pregnancy (12.4 months versus 11.4 months) were similar between both groups

Treatment for RPL with genetic background

Recommendations

All couples with results of an abnormal fetal or parental karyotype should receive genetic counselling.	GPP
All couples with results of an abnormal fetal or parental karyotype may be informed about the possible treatment options available including their advantages and disadvantages.	GPP

TREATMENT FOR WOMEN WITH RPL AND HEREDITARY THROMBOPHILIA

Recommendation		
For women with hereditary thrombophilia and a history of RPL, we suggest not to use antithrombotic prophylaxis unless in the context of research, or if indicated for VTE prevention.	Conditional	⊕⊕■■

TREATMENT FOR WOMEN WITH RPL AND ANTIPHOSPHOLIPID SYNDROME (APS)

Recommendations

For women who fulfil the laboratory criteria of APS and a history of three or more pregnancy losses, we suggest administration with low-dose aspirin (75 to 100 mg/day) starting before conception, and a prophylactic dose heparin (UFH or LMWH) starting at date of a positive pregnancy test, over no treatment.	Conditional	⊕■■■
The GDG suggests offering anticoagulant treatment for women with two pregnancy losses and APS, only in the context of clinical research.	GPP	

Treatment for RPL with immunological background

No immunological biomarker, except for high-titer antiphospholipid antibodies (see chapter 12) can be used for selecting couples with RPL for specific treatments.

TREATMENT FOR THYROID ABNORMALITIES ASSOCIATED WITH RPL

TSH levels should be compared to local trimester-specific reference ranges, or recommended upper limits: e.g. **first** trimester, **2.5** mU/l; **second** trimester, 3.0 mU/l; **third** trimester, **3.5** mU/l

The American Thyroid Association recommends levothyroxine treatment for **pregnant women** with SCH (TSH above trimester specific ranges) and TPOAb, or SCH (with TSH levels above 10.0mU/L),

and recommends to consider treatment for **pregnant women** with TSH concentrations >2.5 mU/L and TPOAb / or TSH >10.0 mU/L. Levothyroxine treatment is not recommended for **TPOAb negative** women with normal TSH

Recommendations (updated 2022)

Overt hypothyroidism arising before conception or during early gestation should be treated with levothyroxine in women with RPL.	Strong	⊕⊕■■
There is conflicting evidence regarding treatment effect of levothyroxine for women with subclinical hypothyroidism and RPL. Treatment of women with SCH may reduce the risk of miscarriage, but the potential benefit of treatment should be balanced against the risks.	Conditional	⊕⊕■■
If women with subclinical hypothyroidism and RPL are pregnant again, TSH level should be checked in early	GPP	

gestation (7-9 weeks gestational age), and hypothyroidism should be treated with levothyroxine.		
If women with thyroid autoimmunity and RPL are pregnant again, TSH level should be checked in early gestation (7-9 weeks gestational age), and hypothyroidism should be treated with levothyroxine.	GPP	
Euthyroid women with thyroid antibodies and RPL should not be treated with levothyroxine.	Strong	⊕⊕⊕■

PROGESTERONE OR (HCG) (FOR LUTEAL PHASE INSUFFICIENCY)

Recommendations

There is insufficient evidence to recommend the use of progesterone to improve live birth rate in women with RPL and luteal phase insufficiency.	Conditional	⊕⊕⊕■
There is insufficient evidence to recommend the use of hCG to improve live birth rate in women with RPL and luteal phase insufficiency.	Conditional	⊕⊕■■

METFORMIN / INSULIN

Recommendation

There is insufficient evidence to recommend metformin supplementation in pregnancy to prevent PL in women with RPL and glucose metabolism defects.	Conditional	⊕■■■

OVULATION INDUCTION

Based on the study of Li, controlled ovarian stimulation by human menopausal gonadotropins could be beneficial for decreasing the chance of a next pregnancy loss in women with RPL diagnosed with luteal phase insufficiency

however the GDG decided that the evidence was too limited to support recommending controlled ovarian stimulation in women with RPL but without PCOS

BROMOCRIPTINE FOR RPL ASSOCIATED WITH HYPERPROLACTINEMIA

In women with RPL and hyperprolactinemia, bromocriptine treatment normalizes serum prolactin levels one single small study showed this treatment to be effective for increasing the chance of a live birth. However, this evidence is not sufficient to recommend the use of bromocriptine in women with RPL and hyperprolactinemia

VITAMIN D

Recommendation

Preconception counselling in women with RPL could include the general advice to consider prophylactic vitamin D supplementation.	GPP

Justification

TREATMENT FOR HYPERHOMOCYSTEINEMIA

In the absence of consistent evidence for an association between HHcy and RPL, assessing Hcy levels is not routinely recommended.

However, if HHcy is detected in women with RPL, treatments are available that can lower Hcy levels and possibly improve the chance of a live birth rate in the next pregnancy

CONGENITAL UTERINE MALFORMATIONS

Recommendations

Only one small RCT showed no benefit of using hysteroscopic septum resection to reduce the rate of pregnancy loss.	Conditional	⊕■■■
Metroplasty is not recommended for bicorporeal uterus with normal cervix (former AFS bicornuate uterus) and RPL.	Strong	⊕■■■
Uterine reconstruction is not recommended for hemi-uterus (former AFS unicornuate uterus) and RPL.	Strong	⊕■■■
There is insufficient evidence in favor of metroplasty in women with bicorporeal uterus and double cervix (former AFS didelphic uterus) and RPL.	Conditional	⊕■■■

ACQUIRED INTRAUTERINE MALFORMATIONS

Recommendations

There is insufficient evidence supporting hysteroscopic removal of submucosal fibroids or endometrial polyps in women with RPL.	Conditional	⊕■■■
Surgical removal of intramural fibroids is not recommended in women with RPL. There is insufficient evidence to recommend removing fibroids that distort the uterine cavity.	Conditional	⊕■■■

Recommendation

There is insufficient evidence of benefit for surgical removal of intrauterine adhesions for pregnancy outcome. After hysteroscopic removal of intrauterine adhesions in women with RPL, precautions have to be taken to prevent recurrence of adhesions.	Conditional	⊕■■■

CERVICAL INSUFFICIENCY

Recommendations

Women with a history of second trimester PLs and suspected cervical weakness should be offered serial cervical sonographic surveillance.	Strong	⊕⊕■■

[129]

In women with a singleton pregnancy and a history of recurrent second-trimester PL attributable to cervical weakness, a cerclage could be considered. There is no evidence that this treatment increases perinatal survival.	Conditional	⊕⊕■■