REVIEW

Prevention

Contraception and cardiovascular disease

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Contraceptive counselling should begin early in females with heart disease, preferably directly after the start of menstruation. In coming to a decision about the method of contraception, the following issues should be considered: (i) the risk of pregnancy for the mother and the consequences of an unplanned pregnancy; (ii) the risks of the contraceptive method; (iii) failure rates; (iv) the non-contraceptive benefits; (v) the availability; (vi) the individual's preferences; (vii) protection against infection; and (viii) costs. In some women with heart disease, the issues may be complex and require the input of both a cardiologist and an obstetrician (or other feto-maternal expert) to identify the optimal approach. No studies have been performed in women with heart disease to investigate the relative risks and benefits of different contraceptive methods.

Introduction

The success of cardiac surgery and the medical management of women with congenital and acquired heart disease means that most will reach puberty and could become pregnant, as most become sexually active even with severe heart disease.[1,2] However, pregnancy is high-risk in at least some of these women and needs careful planning.[1–3] In the large international prospective registry of pregnant patients with cardiac disease (ROPAC), 38% of 1321 women was defined to be high risk and 4% had a contraindication for pregnancy.[2] Effective contraception is essential especially in those with a contraindication for pregnancy. In other women, effective contraception is crucial to allow counselling and optimal timing of pregnancy, improving the chances of an uncomplicated pregnancy. In addition, women with cardiac disease may use medication that is teratogenic (i.e. ACE-inhibitors), consequently, effective contraception is essential. However, the provision of contraceptive advice to these women is sporadic. One study reported that nearly 35% of 49 women had not been advised on the use of contraceptives, while counselling in another 30% had been inappropriate.[4] Another study reported the widespread use of oestrogen-containing formulations (33%), despite their association with an increased risk of thrombo-embolic disease, even in

women with a contraindication for oestrogen-use, while the safer progesterone-only alternatives were used relatively infrequently (1.3%).[5]

Large population-based sexual health studies have all reported a decrease in median age at first intercourse over the past 50–60 years. In the western world, the median age of menarche is around 12–13 and the age at first sexual intercourse for women around 17 years, with 2–30% having sexual intercourse before the age of 15.[6] The mean age at first intercourse of women with heart disease is similar to that of the general population.[7] Clearly general practitioners, (paediatric) cardiologists, obstetricians, and other doctors caring for these women should offer appropriate contraceptive advice early, preferably soon after menstruation starts.

Medically, the key issues relate to reliability and the thrombosis- and infection risk of each possible method. The most reliable methods are those that are the most straight forward to use, the implant and the intrauterine device (IUD). The thrombotic risk is greatest with oestrogen-containing compounds and the copper IUD has the greatest risk of pelvic infection, while all non-barrier contraceptives at best have a limited benefit through thickening of the cervical mucous or not protective benefit at all in preventing infection. A good approach is the use of a long-acting reversible form of contraception combined with a male condom for prevention of sexually transmitted diseases.

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From a health economic perspective, contraception is cost saving to society by preventing the costs and emotional distress associated with unintended pregnancies and terminations.[8] This is even more pronounced in women with medical conditions like heart disease. Subdermal implants, IUDs, and sterilization are more cost effective than other methods.[8] This is related to their contraceptive efficacy, high continuation rate, additional medical benefits (e.g. decreased menstrual bloodloss, low thrombotic risk), and long duration of action.

However, the discussion on contraception should not be limited to the safest and most efficient way to avoid pregnancy, but should encompass other issues like menstrual regulation, reduction of uterine blood loss and menstrual discomfort, as well as the possibility of treatment for endometriosis, PCOS, acne, ovarian cysts, and other conditions. While these issues might be considered less important, they affect the daily comfort and wellbeing of women. The chances of a woman continuing to use contraception are much greater if the method used also makes her feel well.[3] Given the complexity of each request, we prefer an individualized approach where the contraceptive and non-contraceptive benefits and the risks of each method are matched with the patient's desire, after appropriate counselling. In this article, we will discuss the relative risks and benefits of different contraceptive methods in the context of a woman with heart disease.

Type of contraception

To find the best type of contraception, issues such as risks, failure rates, non-contraceptive benefits, individual preferences, and protection against infection should be considered (*Figure 1*).

In some women with heart disease, the issues may be complex and require the input of both a cardiologist and an obstetrician to identify the optimal approach.
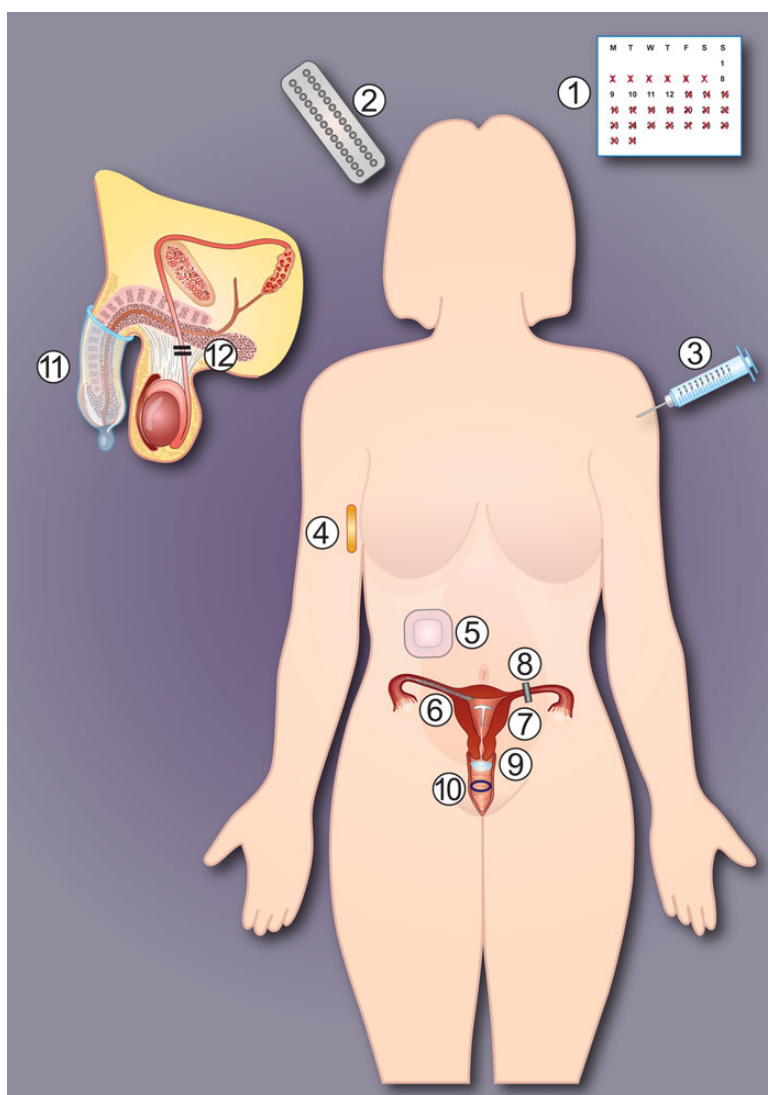
Figure 1 Sketch illustrating different types of contraceptives. (1) Safe period, (2) oral contraceptive (COC or POP), (3) injectable (DMPA), (4) implant, (5) patch, (6) hysteroscopic tubal occlusion, (7) intrauterine contraceptive device, (8) tubal ligation, (9) diaphragm, (10) vaginal ring, (11) male condom, (12) vasectomy.

Table 1 WHO eligibility criteria for widely used contraceptive methods

1	A condition for which there is no restriction for the use of the contraceptive method
2	A condition where the advantages of using the method generally outweigh the theoretical or proven risks
3	A condition where the theoretical or proven risks usually outweigh the advantages of using the method
4	A condition which represents an unacceptable health risk if the contraceptive method is used

The risks and consequences of pregnancy, planned as well as unplanned, can be estimated based upon the Modified WHO classification of maternal cardiovascular risk.[9] For the risks of each contraceptive method, the detailed WHO medical eligibility criteria (WHO-MEC) for contraceptive use offer guidance in women with specific medical conditions.[10] The WHO developed this practical system of recommendations with four categories for each contraceptive method and each medical condition including heart disease (*Table 1*). The guidelines are developed and regularly updated by a panel of international experts, primarily based on scientific evidence where available and expert opinion where it is not. As no studies on contraception have been performed in women with heart disease most recommendations are based on extrapolation of data from studies in women without heart disease. Several national guidelines are based on this system, adapted to the local situation.[11,12]

The efficacy of a contraceptive method is based on its intrinsic mechanism of action, but is also highly dependent on its correct use. It is therefore often expressed as an optimal efficacy, reflecting its theoretical efficacy and a typical efficacy, based on what is observed in real life. *Table 2* shows these efficacies along with the most important risks and benefits.

Barrier methods, calendar methods, and withdrawal

Barrier forms of contraception (including condoms, diaphragms, and cervical caps), calendar methods, or withdrawal before ejaculation are usually considered insufficient due to their substantial failure rate.[13] It consistently seems that humans are not invariably rational or practical when passionate. Nevertheless, a male condom protects against sexually transmitted diseases in non-monogamous relationships and might prove valuable as an additional contraceptive method.

Combined oestrogen and progesterone contraceptives

Combined oestrogen and progesterone contraceptives combine either ethinylestradiol or estradiol valerate with various progestins (progestogens). They are mostly used as tablets with regular stop periods, but they can be delivered by a vaginal ring, injection, or transdermal patch. Combined oral contraceptives are divided in four generations depending on the progestin used and the type and dose of the oestrogen component.

The oestrogen component in combined oral contraceptives significantly increases the risk of venous thrombosis (2−7-fold) irrespective of the type of progestin used although the risk is small in absolute numbers (8−10/10 000 women-years exposure).[15,16] This risk of an unplanned pregnancy must be weighed against the risks of the combined contraceptives. Besides venous thrombosis, combined oral contraceptives increase the risk of arterial thrombosis and hypertension.[17,18] Therefore, combined oral contraceptives are not recommended (WHO-MEC 3) or even contraindicated (WHO-MEC4) in women with cardiac disease (especially those with an increased thrombotic risk, either venous or arterial), ischaemic heart disease or hypertension.

Combined oral contraceptives inhibit ovulation, thicken the cervical mucus, preventing sperm penetration, and prevent implantation by altering endometrial receptivity. Theoretically, contraceptive efficacy is high, but this is completely dependent on its correct usage.[13,19] Some medication may influence their efficacy. For instance, Bosentan, taken in the management of pulmonary hypertension, increases the metabolism of contraceptive steroids, decreasing their efficacy and in this circumstance, a supplementary method, like a condom, should be used.[11,20,21] Combined oral contraceptives usually improve cycle control by making periods regular, less painful, and lighter.[22,23] Women often reduce the frequency of withdrawal bleeds, by continuous intake for 2 or 3 months.[24] Combined oral contraceptives can also be used for the treatment of ovarian cysts, polycystic ovary syndrome, and features of mild hyperandrogenism like acne or hirsutism.[25]

Progesterone-only contraceptives

Progesterone-only methods of contraception come in a variety of formulations.

Depending on the method used, the contraceptive mechanism of action is a combination of cervical mucus thickening, preventing sperm penetration, and reduction of endometrial receptivity, preventing implantation. The higher dose formulations also inhibit ovulation.[19,26−30] Most importantly, progestins probably do not increase the risk of thrombosis, although discussion exists, as some papers have reported an increased risk of thrombosis in patients using Depoprovera, while others have not.[31−34] Progesterone-only pills, commonly known as 'mini-pills' contain various types of progestogens and are used daily without a break. Most have a limited efficacy as contraceptive but were traditionally used as a contraceptive supplement to lactation.

Desogestrel (Cerazette) containing progesterone-only pill is the only one to effectively inhibit ovulation and has a similar safety window (12 h) and contraceptive effectivity as the combined oral contraceptives. It is therefore the only progesterone-only pill recommended in women with (severe) cardiac disease.[11,20,21,28,35] Depot-medroxyprogesterone acetate (DMPA) can be used for intramuscular or subcutaneous injection and offers contraceptive protection for at least 13 weeks. While its effect usually last much longer, adherence to the 13-weekly interval (with a 4-week grace period) is recommended in order to be able to rely on its contraceptive efficacy.[36]

Subdermal implants containing etonogestrel or Levongestrel keep their contraceptive efficacy for 3−5 years and are easily inserted after simple local infiltration in the medial groove between the biceps and

Table 2 The percentage of women who will experience an unplanned pregnancy within the first year of use of a given contraceptive method (typical and optimal usage), together with the percentage of continued use after 1 year, the risk of thrombosis and of infection associated with the method's use. Modified from[13,14]

Group	Contraceptive type	Failure (typical, %)	Failure (optimal, %)	Continued use at 1 year (%)	Thrombosis risk	Infection risk
Highly effective (<1%) Reversible	Implant	0.05	0.05	84	May be slightly increased risk	Minimal
	IUCD	0.2 (LNG)	0.2	80	No increased risk	Transient bacteraemia at insertion, increased PID
		0.8 (Copper)	0.6	78		
Highly effective (<1%) Irreversible	Vasectomy	0.15	0.1	100	No increased risk	Post-operative
	Tubal Occlusion	0.5 (abdominal, laparoscopic, or hysteroscopic)	0.5	100	No increased risk	Post-operative
Moderately effective (3–12%)	Injectable	Depo-Provera 3% Combined injectable 3%	Depo-Provera 0.3% Combined injectable 0.05%	56	Depo-provera: increased risk Combined injectable: increased risk	Minimal, but no protection from PID
	Combined oral contraceptive	8	0.3	68	Increased risk	Minimal, but no protection from PID
	Desogestrel containing progesterone-only pill	8	0.3		No increased risk	Minimal, but no protection from PID
	Patch	8	0.3	68	Increased risk	Minimal, but no protection from PID
	Ring	8	0.3	68	Increased risk	Minimal, but no protection from PID
Poorly effective (18–28%)	Male Condom	15	2	53	No increased risk	Reduced PID
	Diaphragm	16	6	57	No increased risk	Reduced PID
	Female Condom	21	5	49	No increased risk	Reduced PID
	Sponge	16–32 (nulliparous vs. parous)	9–20 (nulliparous vs. parous)	46–57 (parous vs. nulliparous)	No increased risk	No protection from PID
	Safe Period	25	3–5	51	No increased risk	No protection from PID
	Withdrawal	27	4	43	No increased risk	No protection from PID
	Spermicide	29	18	42	No increased risk	No protection from PID
No contraception		85	85			

triceps. The rare failures due to unnoticed loss of the implant at insertion and problems of implant retrieval at removal with the etonogestrel containing implants have largely been overcome by a new inserting device and incorporation of a radioactive filament.[26,36] A large Danish population study including 1 626 158 women, suggested a potential slightly increased thrombotic risk with subdermal implants (relative risk 1.4).[32] However, the study failed to reach statistical significance (95% CI 0.6−3.4).and with other studies assessing the influence on haemostatic parameters being reassuring, there is little evidence of increased thrombosis risk with their use.[32,37−39]

Prolonged exposure to progestagens induces endometrial atrophic changes. This results in an irregular and unpredictable bleeding pattern, often with reduced blood loss, duration, and menstrual frequency (occasionally amenorrhea).[40−43] However, it is also sometimes characterized by continuous spotting.[26,44] The exact mechanism responsible for this remains to be understood but may be related to vascular fragility of the atrophic endometrium.

While most women welcome the reduction in vaginal blood loss, the unpredictable nature or continuous spotting can be bothersome in others. Creating realistic expectations during counselling often greatly contributes to patient satisfaction and acceptance of undesirable side effects.[29,30,45]

Intrauterine contraceptive device and intrauterine system

The two most common forms of reversible intrauterine contraceptives are the banded copper containing intrauterine device (copper-IUD) and Levonogestrel-releasing intrauterine system (IUS) (Levonogestrel-IUS = Mirena). Copper is toxic to the ova and sperm and the device induces an endometrial inflammation preventing implantation, thereby offering safe contraception for 10 years. For the Levonogestrel-IUS, the gradual, local release of progesterone induces endometrial atrophy and the formation of a cervical mucus plug, which impedes sperm penetration offering safe contraception for 5 years. It suppresses ovulation for the 1st two cycles thereafter the cycle returns to normal.[46]

Progesterone containing subdermal implants and Levonogestrel-IUS and copper-IUD are considered long-acting reversible contraceptives. By eliminating the dependency on patient adherence, their efficacy is excellent even exceeding sterilization and fertility rapidly returns upon removal.[13,26,47]

While menstrual blood loss and discomfort might be increased after insertion of a copper-IUD, the Levonogestrel-IUS, after a 3−4-month period of irregular light loss, usually reduces blood loss and, in the majority, results in complete amenorrhea.

An IUD can be used in both nulli- and parous women and have no effect on thrombogenic risk.[48] Insertion is facilitated during menstruation, offering immediate contraception , but can be performed at any point in the cycle and even postpartum.[49] Uterine perforation occurs but is rare.

The risk of pelvic infection is increased for the 3 months after insertion of IUD and women should be warned to report fever or other worrying symptoms promptly. Transient bacteraemia has been documented at replacement but is rare during simple insertion or removal.[50,51] Guidelines for infective endocarditis prophylaxis during placement of these devices has changed considerably over the past decade across Europe and Northern America. The most recent recommendations from the American Heart Association (2008) and the National Institute for Clinical Excellence (2008) no longer advise routine use of antibiotic prophylaxis for genito-urinary instrumentation in women with cardiac disease (including valvular heart disease, congenital heart disease, and cyanotic congenital heart disease) irrespective of their underlying risk of endocarditis, or those with a high risk of adverse outcomes associated with endocarditis.[52,53] These guidelines have been driven by four large randomized trials, which were reviewed in a Cochrane collaboration meta-analysis by Grimes *et al.*[54−58] These randomized controlled trials were designed to explore the peri-procedural infective risk to the upper genito-urinary tract associated with instrumentation during IUD implantation. Pelvic inflammatory disease within 90 days was the primary outcomes in all four trials. Other secondary outcomes included removal of the IUD (in two of the trials) for reasons apart from 'spontaneous' expulsion of the device. Unscheduled visits were another secondary outcome measure. Overall these trials demonstrated that prophylactic doxycycline or azithromycin compared with placebo or no treatment conferred additional benefit (OR 0.89 (95% CI 0.53−1.51).[54] Sinei *et al.*,[56] using doxycycline prophylaxis, showed a significant reduction in non-scheduled visits following IUD insertion in those having received antiobiotic prophylaxis, but failed to show a significant reduction in rates of pelvic inflammatory disease following IUD insertion. Ladipo *et al.*,[55] replicating this methodology in a Nigerian population, were unable to demonstrate any difference in unscheduled visits or infection following IUD insertion. Walsh *et al.*[57] and Zorlu *et al.*[58] also failed to demonstrate any significant benefit for prophylactic antibiotics on pelvic inflammatory disease.

However, a recent retrospective study evaluated the effect on endocarditis prevalence associated with the introduction of the new guidelines over the period 2004−13 (i.e. before and after introduction of the new guidelines). By March 2013, 35 more cases per month of endocarditis were reported than would have been expected.[59] These results do not establish a causal relationship, but call for further systematic evaluation of the specific benefit of antibiotic prophylaxis in high-risk women. Currently, the guidelines states that antibiotic prophylaxis for the placement of an IUD or IUS is not recommended, however, the administration of prophylactic antibiotics (ampicillin 2 g and gentamicin 80 mg given intravenously 1 h before IUCD insertion) prevents bacteraemia and may be wise in high-risk women (e.g. with a prosthetic valve) given the increasing incidence of endocarditis since introduction of the new guidelines, while endocarditis is associated with high morbidity and mortality and the incidence or serious side-effects of prophylactic antibiotics is relatively low.[60]

Sterilization

Sterilization in a patient with a contraindication for pregnancy or after a couple has completed their family is not unreasonable.[11,21,61] Vasectomy, is a highly effective approach to contraception and poses no risk to a woman with heart disease, but may not be ideal in the context of a woman with a high chance of early demise as it compromises the fertility of the man in eventual future relationships. Laparoscopic or open tubal ligation and hysteroscopic insertion of intratubal stents may be the best sterilization option as long as the woman understands

that such procedures should be considered irreversible. If a pregnant woman is to be delivered by caesarean section and has completed her family, then the option of a sterilization at the same time should be discussed mentioning that the regret and failure rate might be slightly higher and the possibility of reversal lower than for the standard laparoscopic approach.[62,63] Not unreasonably, many women are unwilling to be steriliszed as a primary form of contraception, even if they have severe heart disease and pregnancy would carry a very high risk.

Some women will struggle to accept the finality of no longer being able to have children. There are risks associated with the procedure itself and, although rare, it does have a failure rate, and definite adverse effect psychological impact on the patient. Recently, the role of sterilization has been reduced by the availability of other highly reliable and reversible contraceptive techniques, such as subdermal implants and Levonogestrel-IUS.

Emergency contraception

Emergency contraception can be a valuable back-up in case of unprotected intercourse. A single dose of 1.5 mg of Levonogestrel is very efficient with a 1.1% failure rate if taken within 72 h after unprotected intercourse.[64] Its mechanism of action is mainly through delaying ovulation. Therefore, its efficacy is limited once ovulation has occurred.[65] A single dose of Mifeprostone 25 mg and Ulipristal acetate 30 mg, two progesterone receptor modulators, seem to be more effective than Levonogestrel and can be taken up to 120 h after unprotected intercourse. In addition to the inhibition of ovulation, these agents may also prevent implantation and reduce tubal motility.[64–66] Besides minor side effects like nausea, vomiting, and headache, these methods are generally considered safe, even in women with heart disease. Patients should be made aware that menstruation is often delayed. The most effective approach remains the insertion of a copper-IUD within 120 h after intercourse (0.09% failure rate), which, as well as preventing pregnancy, will offer long-term contraception.[67]

Two doses of levonorgestrel (750 μg) have a small effect on blood clotting parameters with an increase in fibrinogen at 24 and 48 h and a reduction in anti-thrombin III lasting from 2–12 h post treatment (oestrogen-based methods have a more marked effect).[68] However, despite these changes, there was no evidence of an increased risk of thrombosis in users of post-coital contraception.[69] On the contrary, a case report described a potentiation of warfarin by levonorgestrel, perhaps by the displacement of warfarin from its main transport protein, α1-acid glycoprotein.[70] Indeed, there may exist a strong and potentially dangerous interaction between high-dose levonorgestrel and warfarin urging the need for extra INR control in the first days. Consequently, it may be better to insert a copper IUD for post-coital contraception in a woman taking warfarin.

Contraceptive advice in women with specific cardiac lesions

There is a paucity of published information and very little evidence about contraception in women with all forms of heart disease. These women are a heterogeneous group, meaning that risk stratification and contraceptive advice has to be individualized and should be based not only on the nature of the cardiac problem, but also on the presence of other medical conditions, the age of the woman and her partner, number of previous children, cultural and religious beliefs, and individual wishes.

Compromised cardiac function

Pregnancy in women with previously diagnosed idiopathic, familial, or peripartum cardiomyopathy carries a risk of heart failure and occasionally death. Deterioration of left-ventricular function is reported in up to 50% of cases in the peripartum period, despite optimal medical therapy.[71,72] Maternal mortality figures typically include deaths that occur during pregnancy or in the first 42 days after delivery. However, deaths related to peripartum cardiomyopathy may occur after this limit and the linkage with the preceding pregnancy lost. The cause of death can be intractable heart failure, sudden death due to ventricular arrhythmia or due to a thrombo-embolic event, occurring as a result of the poorly contractile left and/or right ventricles.[73] Therefore, pregnancy is high-risk in women with a left-ventricular ejection fraction (LVEF) below 45% (WHO Class III) and is contraindicated if LVEF is below 30% (WHO Class IV).[9] In patients with peripartum cardiomyopathy, the occurrence of heart failure has been reported even after a termination of pregnancy or stillbirth, further supporting the need for reliable contraception to prevent unplanned pregnancies. Therefore, in these women, effective contraception is essential and while there is no absolute contraindication to use of any method, an individualized approach should be taken, which includes consideration of the risk of thromboemboli, the use of anticoagulation, and the occurrence of arrhythmias. Although some fluid retention may occur, there is no evidence that the contraceptive steroid hormones aggravate heart failure. However, combined oral contraceptives are contraindicated in women who have a reduced ejection fraction after a myocardial infarction, especially when other risk factors, such as smoking and hypertension, are present.

Contraception in women with heart disease requiring anticoagulation

Women with mechanical valves, Fontan-circulation, and pulmonary hypertension have an increased risk of thrombosis, which is commonly managed using Vitamin K antagonists. In these women, the cardiovascular and thrombogenic risks of (unplanned) pregnancy often outweigh the inherent risks of most contraceptive methods.

However, in women on anticoagulation, the incidence of heavy and prolonged menstrual bleeding as well as intermenstrual and post-coital bleeding is increased.[7,74,75] They can even experience ovarian haemorrhage at ovulation, potentially leading to severe abdominal bleeding on a rare occasion.[76,77]

Both oestrogens and progestins can potentiate the anticoagulative effects of coumarines, necessitating a re-evaluation of the INR several weeks after initiation.[21,70,78] Therefore, in the context of a woman taking anticoagulants, a reliable contraceptive method without increased thrombotic risk, that reduce menstrual blood loss and inhibits ovulation would be most suitable. Progesterone-only methods, especially the long-acting reversible contraceptives and the Levonogestrel-IUS are therefore the method of choice in these women, although being on anticoagulants may increase the tendency

to irregular bleeding patterns, most women would experience a reduction in vaginal blood loss. Indeed, this approach is sometimes used in anticoagulated women solely to reduce menstrual blood loss, despite earlier sterilization.[40–43]

While DMPA injections induces some fluid retention and can be complicated by intramuscular haematoma, it rarely seems to be of clinical significance, even in patients on anticoagulation.[11,20,21,61]

There are no good data on whether the increased thrombogenic risk of combined oral contraceptives is controlled by appropriate anticoagulation.[74,79,80] Given this uncertainty, and the severe consequences of a thrombotic event in this patient population, most guidelines state that combined oral contraceptives are contraindicated (WHO-MEC 4) in women with a history of thrombosis, a mechanical heart valve (particularly the older single leaflet valves like the Bjork Shiley or Starr Edwards), Fontan operation, cyanotic heart disease, pulmonary hypertension, coronary artery disease, or atrial fibrillation despite appropriate anticoagulation.[10–12,21] Nevertheless, there is debate among experts about these recommendations as scientific support is lacking and combined oral contraceptives offer important non-contraceptive benefits such as improved cycle control, particularly in women who wish to discontinue progesterone-only methods due to unpredictable bleeding.[61,81]

While certainly not first choice, we believe that combined oral contraceptives can be considered in these women after appropriate counseling.

Contraceptive interventions in high-risk women

The pain and cervical manipulation during insertion and removal of an IUD can elicit a vagal reaction in as many as 5% of women.[11,20,21,61,79,82] While this is usually benign in most women, it is potentially dangerous in those with pulmonary hypertension or a Fontan repair. Consequently, we recommend that insertion and removal of an IUD in these women occurs in a setting with cardiovascular monitoring, with anaesthetic support on standby, and using appropriate pain relief, either paracervical block or systemic opioids, to prevent a vagal reaction. Taking this into account, Levonogestrel-IUS may therefore be less suited in these women when compared with subdermal implants. Subdermal implants have a superior contraceptive efficacy to sterilization and are easily inserted, only requiring local anaesthetic and are a very option for women with a mechanical valves, pulmonary hypertension, or Fontan repair.[11,20,21,26,29,31,61,83] As in the case of desogestrel containings progresterone-only-pills, these subdermal implants require an additional contraceptive measures in women taking Bosentan.

Sterilization through laparoscopic tubal ligation requires the creation of a pneumoperitioneum and is therefore contraindicated in women with pulmonary hypertension or Fontan repair. If desired, an open or laparoscopic procedure with minimal inflation under general, spinal/epidural, or even local anaesthesia can be considered, but it also requires temporary cessation of the anticoagulation and contains a procedure inherent risk of haemorrhage and thrombosis.[11,21,61,84]

The new methods of tubal occlusion, achieved by hysteroscopic insertion of tubal stents, have been used successfully in a group of women with severe heart disease and may be a good option. Ultrasound assessment of tubal patency after several months is required before effective contraception can be expected.[21,61,85–87] As for IUD insertion, antibiotic coverage can be considered despite the current guidelines and adequate monitoring and pain relief to prevent an eventual vagal reaction should be assured in these women.

Sterilization does not offer the non-contraceptive benefits (e.g. reduction in menstrual blood loss) of other methods. With the contraceptive efficacy of Levonogestrel-IUS and subdermal implants implants exceeding that of sterilization, the indications for the latter is limited in this patient population.

Contraception in women with arrhythmias

Women with arrhythmias often use medication that is teratogenic (i.e. amiodarone), consequently, effective contraception is essential. When a change of antiarrhtyhmic medication is decided upon, it should be implemented when the mother is still using contraception, since this allows time to judge the tolerance and effectiveness of the new medication. In the case of anticoagulant medication, the change can be made in early pregnancy.

A small increase in heart rate was demonstrated in women using oestrogen-containing contraceptives,[88] but not with oestradiol alone.[89] Theoretically, an increase in heart rate could reduce myocardial perfusion and promote cardiac arrhythmias, however, the rise in heart rate in these studies was minor and is therefore unlikely to be of clinical significance. There is no other evidence that contraception of any kind triggers the occurrence of arrhythmias. Therefore, the most important issue is the elevated thrombo-embolic risk with use of combined contraceptives in women with an arrhythmia. In women with isolated arrhythmias (i.e. isolated supraventricular or ventricular extra beats, AVNT, or VT's in long QT-syndrome), combined contraceptives can be used. However, when atrial flutter or fibrillation is present, either paroxysmal or permanent, caution in the use of combined hormonal contraceptives is advised, because of elevated risk of thrombo-embolism (WHO-MEC 3).[11,61,90,91]

Conclusion

Contraception is a delicate, sometimes difficult issue, which carries many ethical, moral, and medical dilemmas. Contraceptive counselling should begin early, and the choice of method based on the impact of (an unplanned) pregnancy, the risks, and benefits of the contraceptive type and the individual's preferences. Complex cases will require the input of both a cardiologist and an obstetrician and the absence of any good quality studies mean that the decision is almost always based on expert opinion. In many situations, the ease of use and efficacy of the progestogen-only long-acting reversible contraceptive methods make them a good method for patients with cardiovascular disease.

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References

1. Baumgartner H, Bonhoeffer P, De Groot NM, de Haan F, Deanfield JE, Galie N, Gatzoulis MA, Gohlke-Baerwolf C, Kaemmerer H, Kilner P, Meijboom F, Mulder BJ, Oechslin E, Oliver JM, Serraf A, Szatmari A, Thaulow E, Vouhe PR, Walma E, Task Force on the Management of Grown-up Congenital Heart Disease of the European Society of C, Association for European Paediatric C, Guidelines ESCCfP. ESC Guidelines for the management of grown-up congenital heart disease (new version 2010). *Eur Heart J* 2010;**31**:2915–2957.

2. Roos-Hesselink JW, Ruys TP, Stein JI, Thilen U, Webb GD, Niwa K, Kaemmerer H, Baumgartner H, Budts W, Maggioni AP, Tavazzi L, Taha N, Johnson MR, Hall R, Investigators R. Outcome of pregnancy in patients with structural or ischaemic heart disease: results of a registry of the European Society of Cardiology. *Eur Heart J* 2013;**34**:657–665.

3. Wellings K, Brima N, Sadler K, Copas AJ, McDaid L, Mercer CH, McManus S, Stephenson J, Glasier A. Stopping and switching contraceptive methods: findings from Contessa, a prospective longitudinal study of women of reproductive age in England. *Contraception* 2015;**91**:57–66.

4. Rogers P, Mansour D, Mattinson A, O'Sullivan JJ. A collaborative clinic between contraception and sexual health services and an adult congenital heart disease clinic. *J Fam Plann Reprod Health Care* 2007;**33**:17–21.

5. Pijuan-Domenech A, Baro-Marine F, Rojas-Torrijos M, Dos-Subira L, Pedrosa-Del Moral V, Subirana-Domenech MT, Goya-Canino M, Cabero-Roura L, Garcia-Dorado D, Casaldaliga-Ferrer J. Usefulness of progesterone-only components for contraception in patients with congenital heart disease. *Am J Cardiol* 2013;**112**:590–593.

6. Mercer CH, Tanton C, Prah P, Erens B, Sonnenberg P, Clifton S, Macdowall W, Lewis R, Field N, Datta J, Copas AJ, Phelps A, Wellings K, Johnson AM. Changes in sexual attitudes and lifestyles in Britain through the life course and over time: findings from the National Surveys of Sexual Attitudes and Lifestyles (Natsal). *Lancet* 2013;**382**:1781–1794.

7. Vigl M, Kaemmerer M, Niggemeyer E, Nagdyman N, Seifert-Klauss V, Trigas V, Bauer U, Schneider KT, Berger F, Hess J, Kaemmerer H. Sexuality and reproductive health in women with congenital heart disease. *Am J Cardiol* 2010;**105**:538–541.

8. Mavranezouli I, Group LGD. The cost-effectiveness of long-acting reversible contraceptive methods in the UK: analysis based on a decision-analytic model developed for a National Institute for Health and Clinical Excellence (NICE) clinical practice guideline. *Hum Reprod* 2008;**23**:1338–1345.

9. European Society of Gynecology (ESC), Association for European Paediatric Cardiology (AEPC), German Society for Gender Medicine (DGesGM), Regitz-Zagrosek V, Blomstrom Lundqvist C, Borghi C, Cifkova R, Ferreira R, Foidart JM, Gibbs JS, Gohlke-Baerwolf C, Gorenek B, Iung B, Kirby M, Maas AH, Morais J, Nihoyannopoulos P, Pieper PG, Presbitero P, Roos-Hesselink JW, Schaufelberger M, Seeland U, Torracca L, Guidelines ESCCfP. ESC Guidelines on the management of cardiovascular diseases during pregnancy: the Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). *Eur Heart J* 2011;**32**:3147–3197.

10. World Health Organization. *Medical Eligibility Criteria for Contraceptive Use: A WHO Family Planning Cornerstone.* 2013/06/07 ed. Geneva; 2010.

11. Thorne S, Nelson-Piercy C, MacGregor A, Gibbs S, Crowhurst J, Panay N, Rosenthal E, Walker F, Williams D, de Swiet M, Guillebaud J. Pregnancy and contraception in heart disease and pulmonary arterial hypertension. *J Fam Plann Reprod Health Care* 2006;**32**:75–81.

12. Centers for Disease Control and Prevention (CDC). U S. Medical Eligibility Criteria for Contraceptive Use, 2010. *MMWR Recomm Rep* 2010;**59**(RR-4):1–86.

13. Trussell J. Contraceptive failure in the United States. *Contraception* 2011;**83**:397–404.

14. WHO. *Medical eligibility criteria for contraceptive use*, 4th ed. WHO Library Cataloguing-in-Publication Data: WHO Press; 2010.

15. Lidegaard O, Lokkegaard E, Svendsen AL, Agger C. Hormonal contraception and risk of venous thromboembolism: national follow-up study. *BMJ* 2009;**339**:b2890.

16. Dinger J, Bardenheuer K, Heinemann K. Cardiovascular and general safety of a 24-day regimen of drospirenone-containing combined oral contraceptives: final results from the International Active Surveillance Study of Women Taking Oral Contraceptives. *Contraception* 2014;**89**:253–263.

17. Lidegaard O, Lokkegaard E, Jensen A, Skovlund CW, Keiding N. Thrombotic stroke and myocardial infarction with hormonal contraception. *N Engl J Med* 2012;**366**:2257–2266.

18. Dong W, Colhoun HM, Poulter NR. Blood pressure in women using oral contraceptives: results from the Health Survey for England 1994. *J Hypertens* 1997;**15**:1063–1068.

19. Milsom I, Korver T. Ovulation incidence with oral contraceptives: a literature review. *J Fam Plann Reprod Health Care* 2008;**34**:237–246.

20. Mohan AR, Nelson-Piercy C. Drugs and therapeutics, including contraception, for women with heart disease. *Best Pract Res Clin Obstet Gynaecol* 2014;**28**:471–482.

21. Thorne S, MacGregor A, Nelson-Piercy C. Risks of contraception and pregnancy in heart disease. *Heart* 2006;**92**:1520–1525.

22. Kaunitz AM. Oral contraceptive health benefits: perception versus reality. *Contraception* 1999;**59**(Suppl.):29S–33S.

23. Sulak PJ, Scow RD, Preece C, Riggs MW, Kuehl TJ. Hormone withdrawal symptoms in oral contraceptive users. *Obstet Gynecol* 2000;**95**:261–266.

24. Anderson FD. Safety and efficacy of an extended-regimen oral contraception utilizing low-dose ethinyl estradiol. *Contraception* 2006;**74**:355.

25. Dragoman MV. The combined oral contraceptive pill- recent developments, risks and benefits. *Best Pract Res Clin Obstet Gynaecol* 2014;**28**:825–834.

26. Espey E, Ogburn T. Long-acting reversible contraceptives: intrauterine devices and the contraceptive implant. *Obstet Gynecol* 2011;**117**:705–719.

27. Hurskainen R, Paavonen J. Levonorgestrel-releasing intrauterine system in the treatment of heavy menstrual bleeding. *Curr Opin Obstet Gynecol* 2004;**16**:487–490.

28. Korver T, Klipping C, Heger-Mahn D, Duijkers I, van Osta G, Dieben T. Maintenance of ovulation inhibition with the 75-microg desogestrel-only contraceptive pill (Cerazette) after scheduled 12-h delays in tablet intake. *Contraception* 2005;**71**:8–13.

29. Mansour D, Bahamondes L, Critchley H, Darney P, Fraser IS. The management of unacceptable bleeding patterns in etonogestrel-releasing contraceptive implant users. *Contraception* 2011;**83**:202–210.

30. Mansour D, Korver T, Marintcheva-Petrova M, Fraser IS. The effects of Implanon on menstrual bleeding patterns. *Eur J Contracept Reprod Health Care* 2008;**13**(Suppl. 1):13–28.

31. Lidegaard O, Nielsen LH, Skovlund CW, Skjeldestad FE, Lokkegaard E. Risk of venous thromboembolism from use of oral contraceptives containing different progestogens and oestrogen doses: Danish cohort study, 2001–9. *BMJ* 2011;**343**:d6423.

32. Lidegaard O, Nielsen LH, Skovlund CW, Lokkegaard E. Venous thrombosis in users of non-oral hormonal contraception: follow-up study, Denmark 2001–10. *BMJ* 2012;**344**:e2990.

33. Mantha S, Karp R, Raghavan V, Terrin N, Bauer KA, Zwicker JI. Assessing the risk of venous thromboembolic events in women taking progestin-only contraception: a meta-analysis. *BMJ* 2012;**345**:e4944.

34. Goldstein J, Cushman M, Badger GJ, Johnson JV. Effect of depomedroxyprogesterone acetate on coagulation parameter: a pilot study. *Fertil Steril* 2007;**87**:1267–1270.

35. Wald RM, Sermer M, Colman JM. Pregnancy and contraception in young women with congenital heart disease: General considerations. *Paediatr Child Health* 2011;**16**:e25–e29.

36. Jacobstein R, Polis CB. Progestin-only contraception: injectables and implants. *Best Pract Res Clin Obstet Gynaecol* 2014;**28**:795–806.

37. Vieira CS, Ferriani RA, Garcia AA, Pintao MC, Azevedo GD, Gomes MK, Silva-de-Sa MF. Use of the etonogestrel-releasing implant is associated with hypoactivation of the coagulation cascade. *Hum Reprod* 2007;**22**:2196–2201.

38. Vieira CS, Ferriani RA, Garcia AA, Gomes MK, Azevedo GD, Silva de Sa MF. Transitory reduction of platelet aggregation with the use of etonogestrel implant in healthy women. *Thromb Haemost* 2005;**94**:682–683.

39. Brito MB, Ferriani RA, Meijers JC, Garcia AA, Quintana SM, Silva de Sa MF, Vieira CS. Effects of the etonogestrel-releasing contraceptive implant inserted immediately postpartum on maternal hemostasis: a randomized controlled trial. *Thromb Res* 2012;**130**:355–360.

40. Culwell KR, Curtis KM. Use of contraceptive methods by women with current venous thrombosis on anticoagulant therapy: a systematic review. *Contraception* 2009;**80**:337–345.

41. Kadir RA, Chi C. Levonorgestrel intrauterine system: bleeding disorders and anticoagulant therapy. *Contraception* 2007;**75**(Suppl.):S123–S129.

42. Pisoni CN, Cuadrado MJ, Khamashta MA, Hunt BJ. Treatment of menorrhagia associated with oral anticoagulation: efficacy and safety of the levonorgestrel releasing intrauterine device (Mirena coil). *Lupus* 2006;**15**:877–880.

43. Saha PK, Rakshit BM, Jana N, Dutta S, Roy SB, Sengupta G. Management of abnormal uterine bleeding in women with mechanical heart valve prosthesis and anticoagulant therapy. *J Indian Med Assoc* 2011;**109**:908–911.

44. Sordal T, Inki P, Draeby J, O'Flynn M, Schmelter T. Management of initial bleeding or spotting after levonorgestrel-releasing intrauterine system placement: a randomized controlled trial. *Obstet Gynecol* 2013;**121**:934–941.

45. Modesto W, Bahamondes MV, Bahamondes L. A randomized clinical trial of the effect of intensive versus non-intensive counselling on discontinuation rates due to bleeding disturbances of three long-acting reversible contraceptives. *Hum Reprod* 2014;**29**:1393–1399.

46. Stephen Searle E. The intrauterine device and the intrauterine system. *Best Pract Res Clin Obstet Gynaecol* 2014;**28**:807–824.

47. Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention (CDC). U.S. Selected Practice Recommendations for Contraceptive Use, 2013: adapted from the World Health Organization selected practice recommendations for contraceptive use, 2nd edition. *MMWR Recomm Rep* 2013;**62**(RR-05):1–60.

48. Bahamondes MV, Hidalgo MM, Bahamondes L, Monteiro I. Ease of insertion and clinical performance of the levonorgestrel-releasing intrauterine system in nulligravidas. *Contraception* 2011;**84**:e11–e16.

49. Kapp N, Curtis KM. Intrauterine device insertion during the postpartum period: a systematic review. *Contraception* 2009;**80**:327–336.

50. Murray S, Hickey JB, Houang E. Significant bacteremia associated with replacement of intrauterine contraceptive device. *Am J Obstet Gynecol* 1987;**156**:698–700.

51. Everett ED, Reller LB, Droegemueller W, Greer BE. Absence of bacteremia after insertion or removal of intrauterine devices. *Obstetr Gynecol* 1976;**47**:207–209.

52. Nishimura RA, Carabello BA, Faxon DP, Freed MD, Lytle BW, O'Gara PT, O'Rourke RA, Shah PM. ACC/AHA 2008 Guideline update on valvular heart disease: focused update on infective endocarditis: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines endorsed by the Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2008;**52**:676–685.

53. Centre for Clinical Practice at NICE (UK). *Prophylaxis Against Infective Endocarditis: Antimicrobial Prophylaxis Against Infective Endocarditis in Adults and Children Undergoing Interventional Procedures.* London: National Institute for Health and Clinical Excellence (UK); 2008.

54. Grimes DA, Schulz KF. Antibiotic prophylaxis for intrauterine contraceptive device insertion. *Cochrane Database Syst Rev* 2001;CD001327.

55. Ladipo OA, Farr G, Otolorin E, Konje JC, Sturgen K, Cox P, Champion CB. Prevention of IUD-related pelvic infection: the efficacy of prophylactic doxycycline at IUD insertion. *Adv Contracept* 1991;**7**:43–54.

56. Sinei SK, Schulz KF, Lamptey PR, Grimes DA, Mati JK, Rosenthal SM, Rosenberg MJ, Riara G, Njage PN, Bhullar VB, Ogembo HV. Preventing IUCD-related pelvic infection: the efficacy of prophylactic doxycycline at insertion. *Br J Obstet Gynaecol* 1990;**97**:412–419.

57. Walsh TL, Bernstein GS, Grimes DA, Frezieres R, Bernstein L, Coulson AH. Effect of prophylactic antibiotics on morbidity associated with IUD insertion: results of a pilot randomized controlled trial. IUD Study Group. *Contraception* 1994;**50**:319–327.

58. Zorlu CG, Aral K, Cobanoglu O, Gurler S, Gokmen O. Pelvic inflammatory disease and intrauterine devices: prophylactic antibiotics to reduce febrile complications. *Adv Contracept* 1993;**9**:299–302.

59. Dayer MJ, Jones S, Prendergast B, Baddour LM, Lockhart PB, Thornhill MH. Incidence of infective endocarditis in England, 2000–13: a secular trend, interrupted time-series analysis. *Lancet* 2015;**385**:1219–1228.

60. Suri V, Aggarwal N, Kaur R, Chaudhary N, Ray P, Grover A. Safety of intrauterine contraceptive device (copper T 200 B) in women with cardiac disease. *Contraception* 2008;**78**:315–318.

61. Silversides CK, Sermer M, Siu SC. Choosing the best contraceptive method for the adult with congenital heart disease. *Curr Cardiol Rep* 2009;**11**:298–305.

62. Hillis SD, Marchbanks PA, Tylor LR, Peterson HB. Poststerilization regret: findings from the United States Collaborative Review of Sterilization. *Obstet Gynecol* 1999;**93**:889–895.

63. Peterson HB, Xia Z, Hughes JM, Wilcox LS, Tylor LR, Trussell J. The risk of pregnancy after tubal sterilization: findings from the U.S. Collaborative Review of Sterilization. *Am J Obstet Gynecol* 1996;**174**:1161–1168. discussion 1168–1170.

64. Cheng L, Che Y, Gulmezoglu AM. Interventions for emergency contraception. *Cochrane Database Syst Rev* 2012;**8**:CD001324.

65. Li HW, Lo SS, Ho PC. Emergency contraception. *Best Pract Res Clin Obstet Gynaecol* 2014;**28**:835–844.

66. Glasier AF, Cameron ST, Fine PM, Logan SJ, Casale W, Van Horn J, Sogor L, Blithe DL, Scherrer B, Mathe H, Jaspart A, Ulmann A, Gainer E. Ulipristal acetate versus levonorgestrel for emergency contraception: a randomised non-inferiority trial and meta-analysis. *Lancet* 2010;**375**:555–562.

67. Cleland K, Zhu H, Goldstuck N, Cheng L, Trussell J. The efficacy of intrauterine devices for emergency contraception: a systematic review of 35 years of experience. *Hum Reprod* 2012;**27**:1994–2000.

68. van Rooijen M, Silveira A, Thomassen S, Hansson LO, Rosing J, Hamsten A, Bremme K. Rapid activation of haemostasis after hormonal emergency contraception. *Thromb Haemost* 2007;**97**:15–20.

69. Vasilakis C, Jick SS, Jick H. The risk of venous thromboembolism in users of postcoital contraceptive pills. *Contraception* 1999;**59**:79–83.

70. Ellison J, Thomson AJ, Greer IA, Walker ID. Drug points: apparent interaction between warfarin and levonorgestrel used for emergency contraception. *BMJ* 2000;**321**:1382.

71. Forster O, Hilfiker-Kleiner D, Ansari AA, Sundstrom JB, Libhaber E, Tshani W, Becker A, Yip A, Klein G, Sliwa K. Reversal of IFN-gamma, oxLDL and prolactin serum levels correlate with clinical improvement in patients with peripartum cardiomyopathy. *Eur J Heart Fail* 2008;**10**:861–868.

72. Elkayam U, Tummala PP, Rao K, Akhter MW, Karaalp IS, Wani OR, Hameed A, Gviazda I, Shotan A. Maternal and fetal outcomes of subsequent pregnancies in women with peripartum cardiomyopathy. *N Engl J Med* 2001;**344**:1567–1571.

73. Sliwa K, Libhaber E, Elliott C, Momberg Z, Osman A, Zuhlke L, Lachmann T, Nicholson L, Thienemann F, Roos-Hesselink J, Anthony J. Spectrum of cardiac disease in maternity in a low-resource cohort in South Africa. *Heart* 2014;**100**:1967–1974.

74. Huq FY, Tvarkova K, Arafa A, Kadir RA. Menstrual problems and contraception in women of reproductive age receiving oral anticoagulation. *Contraception* 2011;**84**:128–132.

75. Zingone MM, Guirguis AB, Airee A, Cobb D. Probable drug interaction between warfarin and hormonal contraceptives. *Ann Pharmacother* 2009;**43**:2096–2102.

76. Canobbio MM, Perloff JK, Rapkin AJ. Gynecological health of females with congenital heart disease. *Int J Cardiol* 2005;**98**:379–387.

77. Gupta N, Dadhwal V, Deka D, Jain SK, Mittal S. Corpus luteum hemorrhage: rare complication of congenital and acquired coagulation abnormalities. *J Obstet Gynaecol Res* 2007;**33**:376–380.

78. de Teresa E, Vera A, Ortigosa J, Pulpon LA, Arus AP, de Artaza M. Interaction between anticoagulants and contraceptives: an unsuspected finding. *Br Med J* 1979;**2**:1260–1261.

79. Ott J, Promberger R, Kaufmann U, Huber JC, Frigo P. Venous thrombembolism, thrombophilic defects, combined oral contraception and anticoagulation. *Arch Gynecol Obstet* 2009;**280**:811–814.

80. Comp PC, Zacur HA. Contraceptive choices in women with coagulation disorders. *Am J Obstet Gynecol* 1993;**168**(Pt 2):1990–1993.

81. ACOG Committee on Practice Bulletins-Gynecology. ACOG practice bulletin. No. 73: Use of hormonal contraception in women with coexisting medical conditions. *Obstet Gynecol* 2006;**107**:1453–1472.

82. Gemzell-Danielsson K, Mansour D, Fiala C, Kaunitz AM, Bahamondes L. Management of pain associated with the insertion of intrauterine contraceptives. *Hum Reprod Update* 2013;**19**:419–427.

83. Aznar R, Reynoso L, Ley E, Gamez R, De Leon MD. Electrocardiographic changes induced by insertion of an intrauterine device and other uterine manipulations. *Fertil Steril* 1976;**27**:92–96.

84. Snabes MC, Poindexter AN III. Laparoscopic tubal sterilization under local anesthesia in women with cyanotic heart disease. *Obstet Gynecol* 1991;**78**(Pt 1):437–440.

85. Duffy S, Marsh F, Rogerson L, Hudson H, Cooper K, Jack S, Hunter D, Philips G. Female sterilisation: a cohort controlled comparative study of ESSURE versus laparoscopic sterilisation. *BJOG* 2005;**112**:1522–1528.

86. Famuyide AO, Hopkins MR, El-Nashar SA, Creedon DJ, Vasdev GM, Driscoll DJ, Connolly HM, Warnes CA. Hysteroscopic sterilization in women with severe cardiac disease: experience at a tertiary center. *Mayo Clin Proc* 2008;**83**:431–438.

87. Kerin JF, Cooper JM, Price T, Herendael BJ, Cayuela-Font E, Cher D, Carignan CS. Hysteroscopic sterilization using a micro-insert device: results of a multicentre Phase II study. *Hum Reprod* 2003;**18**:1223–1230.

88. Cagnacci A, Zanin R, Napolitano A, Arangino S, Volpe A. Modification of 24-h ambulatory blood pressure and heart rate during contraception with the vaginal ring: a prospective study. *Contraception* 2013;**88**:539–543.

89. Grandi G, Xholli A, Napolitano A, Piacenti I, Bellafronte M, Cagnacci A. Prospective measurement of blood pressure and heart rate over 24 h in women using combined oral contraceptives with estradiol. *Contraception* 2014;**90**:529–534.

90. European Heart Rhythm Association, European Association for Cardio-Thoracic Surgery, Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S, Van Gelder IC, Al-Attar N, Hindricks G, Prendergast B, Heidbuchel H, Alfieri O, Angelini A, Atar D, Colonna P, De Caterina R, De Sutter J, Goette A, Gorenek B, Heldal M, Hohloser SH, Kolh P, Le Heuzey JY, Ponikowski P, Rutten FH. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J* 2010;**31**:2369–2429.

91. Camm AJ, Lip GY, De Caterina R, Savelieva I, Atar D, Hohnloser SH, Hindricks G, Kirchhof P, Guidelines ESCCfP. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation. Developed with the special contribution of the European Heart Rhythm Association. *Eur Heart J* 2012;**33**:2719–2747.