

• 专家共识 •

《中国心肺复苏专家共识》之孕产妇心搏骤停防治救指南

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【摘要】 孕妇作为特殊时期的一组人群,一旦出现突发心搏骤停(CA)会威胁到母子两人的生命。最大限度地降低孕产妇死亡,确保围产期母子全程平安,成为医疗机构和医护人员要面对的巨大挑战。与相同年龄普通 CA 患者的心肺复苏施救策略不同,孕期 CA 患者施救需要考虑患者的孕龄、胎儿情况等,采用不同的复苏手法如左推子宫(MLUD),会涉及濒死剖宫产(PMCD);同时针对导致孕期 CA 的不同原因如出现 4Hs 中的低氧血症、低血容量、高血钾或低血钾及其他电解质紊乱、低体温,以及 4Ts 中的血栓形成、心包填塞、张力性气胸和中毒等情况的合理药物应用。针对导致孕期 CA 的原因中多种情况为可预防性的特点,更有必要出台符合我们国情的孕期 CA 指南以指导临床。本文系统梳理了孕期 CA 的病理生理特点,孕期 CA 的高危因素,明确了孕期 CA 的正确复苏方法和防治策略。

【关键词】 孕期; 心搏骤停; 心肺复苏; 病因; 预防

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Chinese consensus of cardiopulmonary resuscitation guides prevention, treatment and rescue of cardiac arrest in pregnancy

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【Abstract】 Pregnant women are a group of people in a special period, once sudden cardiac arrest (CA) occurs, it will threaten the life of both mother and child. It has become a great challenge for hospital, doctors and nurses to minimize maternal mortality during pregnancy. All the efforts should ensure the safety of both mother and child throughout the perinatal period. Because difference of the cardiopulmonary resuscitation strategies for common CA patients of the same age, the resuscitation strategies for CA patients during pregnancy need consider the patient's gestational age and fetal condition. Different resuscitation techniques, such as manual left uterine displacement (MLUD), will involve perimortem cesarean delivery (PMCD). At the same time, drugs should be reasonably used for different causes of CA during pregnancy, such as hypoxemia, hypovolemia, hyperkalemia or hypokalemia and other electrolyte disorders and hypothermia in 4Hs, as well as thrombosis, pericardial tamponade, tension pneumothorax and toxicosis in 4Ts. In view of the fact that many causes of CA in pregnancy are preventable, it is more necessary to introduce guidelines for CA in pregnancy in line with our national conditions for clinical guidance. This paper systematically reviewed the pathophysiological characteristics of CA during pregnancy, the high-risk factors of CA during pregnancy, and identified the correct resuscitation methods and prevention and treatment strategies of CA during pregnancy.

【Key words】 Pregnancy; Cardiac arrest; Cardiopulmonary resuscitation; Etiology; Prevention

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孕妇作为特殊时期的一组人群,尽管出现突发心搏骤停(cardiac arrest, CA)概率非常低,但因会殃及到母子两人的生命,危害性极大^[1]。最大限度地降低孕、产妇死亡率,确保围产期母子全程平安成为医疗机构和医护人员面对的巨大挑战。幸运的是,导致孕期 CA 的原因中多种情况是可以预防,甚至是可以有效避免的。孕妇出现 CA 的准确识别、有效的气道管理及结合手动将子宫推向左侧(左推子宫,即 manual left uterine displacement, MLUD)的精准心肺复苏(cardiopulmonary resuscitation, CPR)手法^[2]、妊娠合并子痫治疗、依据胎龄决策的濒死期

剖宫产(perimortem cesarean delivery, PMCD)术及是否取舍胎儿等都是孕期 CA 需要关注的重要问题。我国二胎政策的放开、大龄或者高危妊娠数量随之增加,迫切需要出台孕期 CA 相关的诊疗规范。欧洲心脏病协会(European Society of Cardiology, ESC)在 2003 年曾经出台了孕期心血管疾病管理^[3],并先后于 2011 年^[4]和 2018 年^[5]从不同角度,如诊断技术、危险分层、心血管药物应用等循证医学证据做出进一步的更新。我国目前尚缺乏有说服力的、系统的孕妇 CA 诊治的共识或指南且相对陈旧^[6-7]。鉴于此,本文整合了 2012 至 2015 年 ESC 发布的



指南中涉及的先天性心脏病(先心病)、主动脉疾病、瓣膜病、心肌病、心力衰竭(心衰)、冠状动脉疾病(coronary artery disease, CAD)、高血压、心包疾病、肺栓塞(pulmonary embolism, PE)、肺动脉高压(pulmonary hypertension, PAH)、感染性心内膜炎、室性心律失常、急性冠脉综合征(acute coronary syndrome, ACS)和 2016 年发布的肿瘤治疗及其心脏毒性、血脂代谢紊乱、心房颤动(房颤)及心血管疾病预防等方面,融合了孕期发生 CA 的病理生理、孕期防控 CA 的高危因素、孕期救治 CA 的 CPR 方法、孕期预防 CA 的防治规范,对孕期发生 CA 的常见疾病、预防及处理进行梳理成篇,体现着上防“未心”、中治“欲心”、下救“已心”的理念。中国研究型医院学会心肺复苏专业专业委员会,中国老年保健协会心肺复苏专业委员会,中国健康管理协会健康文化委员会,中华医学会科学普及分会,北京医学会灾难医学与心肺复苏专业委员会在系列出台相关的《中国心肺复苏专家共识》之后^[8-12],颁布了 2022 中国孕产妇 CA 防治指南,供同道们参考。

1 孕期发生 CA 的病理生理

孕期 CA 是指在怀孕的任何阶段和胎儿娩出后 6 周内发生的 CA。各个国家的流行病学资料数据略有区别:英国研究资料显示孕期 CA 的发生率是 1/36 000^[13]。孕产妇死亡率仍然很高,2017 年估计有 29.5 万例死亡,其中大多数(94%)发生在低收入和中低收入国家^[14]。美国 1998 至 2011 年的研究数据显示,住院期间分娩的孕妇 CA 的发生率大概为 1/12 000^[15]。孕产妇 CA 的预后在很大程度上取决于原发病是否得到控制,积极治疗诱因解除之后存活率高达 58%。但是,来自美国疾病控制与预防中心(the Centers for Disease Control, CDC)数据显示,孕产妇死亡率由 1987 年的 7.2/10 万,上升至 2013 年的 17.3/10 万^[1],部分原因可能是美国女性生育年龄偏大,且较多数量的孕妇患有心脏风险因素^[16],导致孕期 CA 原因中排在前列的有围产期心肌病(peripartum cardiomyopathy, PPCM)、主动脉疾病、急性心肌梗死(acute myocardial infarction, AMI)等^[17-20]。

了解孕期母体病理生理变化的特殊性,有助于在更加有效的 CPR 施救过程中避免发生意外。孕期存在的病理生理变化是多系统的:①生理性贫血会不同程度地降低氧输送能力^[21]。②怀孕期间血浆容量增加由妊娠 12 周时的 15% 升至妊娠晚期的 50%^[22],而其中 75% 的增加发生在妊娠分娩前

3 个月结束。③心排血量的增加是通过怀孕前半期心搏量的增加和孕后期心率的增加来实现的,患有心脏病的妇女中,左心室(left ventricle, LV)和右心室(right ventricle, RV)对怀孕期间的适应性变化存在局限^[23-26]。④孕期全身和肺血管阻力降低加之怀孕期间处于高凝状态,成为增加血栓栓塞风险的重要因素。母体心功能障碍与子宫胎盘血流受损和胎儿预后不佳有关^[25-27]。⑤妊娠 6 周开始出现全身血管阻力降低,容易导致血压降低。⑥妊娠后期产妇的心率每分钟增加 20%~30% 或 15~20 次,每分钟心排血量会代偿性增加 30%~50% 或 1.8 L,子宫接收约 17% 的产妇心排血量^[28-31]。⑦增大的子宫引起主腔静脉的压迫,导致心脏前负荷降低,出现低血压和心动过缓(仰卧位时加剧)的风险,横膈抬高可达 4 cm,导致胸部顺应性降低,仰卧位时肺的功能残气量降低高达 25%,从而大大降低了氧气储备功能^[32]。⑧孕酮水平升高也会导致孕妇的分钟通气量增加,表现为轻度呼吸性碱中毒。孕酮水平升高也会导致上呼吸道黏膜充血,极易因呼吸道感染导致相对的通气量不足。⑨随着孕龄增加,膈肌上抬、胃排空延迟、食管下括约肌松弛,增加了复苏期间误吸风险^[22]。⑩肝酶系统活性的增加,肾小球滤过率、血浆容量、蛋白质结合改变和血清白蛋白水平的降低都会影响许多药物的药代动力学改变^[26, 33]。⑪子宫收缩、体位(左侧或仰卧位)、疼痛、焦虑、用力、出血和子宫复原会在分娩及产后期间引起显著的血流动力学变化。麻醉、出血和感染可引起额外的心血管系统改变。

2 孕期防控 CA 的高危因素

与普通成人 CA 的因素略有不同,孕产妇 CA 常常是产妇心源性猝死的直接且首要原因,常见的因素包括孕期或者产时的原因〔如产后出血、产前出血、心脏疾病、羊水栓塞(amniotic fluid embolism, AFE)、脓毒症〕和孕妇本身合并的已知或者未知的疾病(如心肌病、先心病、心衰、瓣膜病、结缔组织病)等。据统计,全球每年大约有 800 例孕产妇死亡。2011 至 2013 年,美国孕产妇主要的死亡原因为心血管因素,其次为非心血管因素、感染和出血。同样,2013 至 2015 年,英国孕产妇主要死亡原因也是心血管因素。麻醉导致的孕产妇死亡比例呈逐渐下降趋势。研究显示约有 1%~4% 妊娠合并母体疾病,目前孕期 CA 与怀孕有关心脏病的流行率和发病率的数据在全球范围内均很有限。来自英国的研究显示,

成人猝死综合征、PPCM、主动脉夹层(aorta dissection, AD)和 AMI 是孕产妇死亡的常见原因^[16-19, 34]。来自西方 10 个国家的统计资料显示,初次怀孕年龄的增加(约 28.8~31.2 岁)伴随着孕期心血管疾病风险的增加^[16-19, 34-35]。生育后期(或者 40~50 岁)CA 的发生往往与心血管危险因素的发病率增加有关,特别是糖尿病、高血压和肥胖^[16-19, 34]。孕期高血压(发生率 5%~10%)也已成为心血管功能紊乱的常见原因。先心病是西方国家妊娠期间最常见的心血管疾病(75%~82%)^[16-19, 34, 36-37]。风湿性瓣膜病在非西方国家占主导地位,占妊娠期所有心血管疾病的 56%~89%^[16-19, 34, 38]。心肌病相对少见,一旦发生往往代表严重的心血管并发症^[16-19, 34, 39]。

另有研究显示^[16-19, 34],导致孕期 CA 的疾病及其比例分别为:心脏源性疾病(23%)、栓塞性疾病(16%)、癫痫或卒中(13%)、脓毒症(10%)、精神心理性疾病(10%)、出血(8%)、肿瘤(4%)及先兆子痫(2%)。其风险随着年龄增长、社会及种族等因素有升高趋势。2011 至 2014 年可识别的孕妇 CA 患者中 66 例死亡 28 例(42%),其中约 25%(16 例)的 CA 与麻醉有关(12 例为肥胖),且全部存活^[40]。孕期 CA 在 CPR 过程中,重要的是设法寻找可逆的原因。比较容易掌握的病因如 4Hs 中低氧血症、低血容量、高血钾低血钾及其他电解质紊乱、低体温,以及 4Ts 中血栓形成、心包填塞、张力性气胸和中毒^[2, 16-19, 34]。孕期特有的导致 CA 的疾病如异位妊娠、胎盘早剥或子宫破裂^[16-19, 34, 40-41]。孕妇还可以存在同年组可能会合并的导致 CA 的疾病,如过敏、药物过量、创伤等;危及生命的出血相关疾病可以出现在产前,也可以发生在产后^[16-19, 34, 42]。

3 孕期救治 CA 的复苏方法

3.1 孕妇 CA 的救治原则:与非孕成人 CPR 相同,主要包括基础生命支持(basic life support, BLS)和高级生命支持(advanced life support, ALS)。BLS 主要是指对 CA 的孕妇进行有效胸外心脏按压,可行电除颤、气道开放及机械通气治疗等。ALS 是使孕妇恢复自主循环,次级目标是减少患者神经系统损伤,终极目标是提高患者出院存活率。

3.2 孕妇 CA 复苏流程:BLS 的具体方法与同龄非孕成人相同,按压与通气比例为 30:2,按压频率为 100~120 次/min,按压部位为胸骨中下段(或两乳头连线与胸骨交叉处,无需上提按压点),按压深度为 5~6 cm,同时确保胸廓充分回弹^[43]。需要注

意的是,孕期 CPR 建议徒手施救而不建议机械按压^[44-45]。基于孕妇的呼吸道病理生理变化,CPR 过程中需要警惕胃食管反流,以免增加气管插管失败率及误吸风险的发生^[46-48]。孕期 CA 的气道管理需要遵从指南中 ALS 的步骤,规范使用储氧面罩 100% 吸氧(Flow 15 L/min)、严格气道管理,必要时给予气管插管^[48]。

3.3 孕妇 CA 的特殊手法——左推子宫(MLUD;图 1):患者处于平卧位,施救者用手将孕妇子宫推向左侧,确保最大限度地避免主动脉和下腔静脉受压^[49-50]。这种特殊动作还可用于预防孕期 CA 的低血容量或者休克的发生^[51-53]。



图 1 孕妇复苏期间手动左推子宫示意图^[53]

3.4 其 他

3.4.1 按压期间转运问题:由于转运至手术室可能降低孕产妇 CPR 的成功率,考虑到即刻剖宫产的必要性,建议就地(床旁)实施 CPR,无需转运至手术室。

3.4.2 濒死剖宫产(perimortem cesarean delivery, PMCD):PMCD 是在 CPR 期间对孕妇实施剖宫产,是孕妇 CA 时进行 ALS 的重要环节。PMCD 的定义是产妇 CA 后分娩胎儿应在复苏失败 4 min 后开始,目标是在复苏努力开始后 5 min 内分娩^[54],包括产妇复苏、剖宫产和新生儿复苏三部分,最好在 5 min 内完成,并在有经验的医院进行^[55-57]。抢救团队由产科、新生儿科、麻醉科和相关的 CA 救援小组共同组成。如果母亲有明显的无法生存的迹象,就没有必要等待 PMCD。实施 PMCD 应注意以下情况^[2]:
① 如果胎儿胎龄<20 周,不必考虑紧急剖宫产,可直接行 CPR,因为此时子宫大小尚不能对母体心

排血量产生明显影响。② 如果胎儿胎龄处于 20 ~ 23 周,实施 PMCD 有助于母体复苏成功而不是抢救胎儿,因为该时段胎龄的胎儿不可能存活。③ 如果胎儿胎龄处于 24 ~ 25 周,实施 PMCD 有助于同时抢救母婴,有时甚至需要同时行紧急子宫切除术。总之,施行 PMCD 的时间越快越好。由于催产素有可能导致 CA,需谨慎使用^[58]。

3.4.3 除颤: 尽早给予电除颤而非血压测不出再开始。除颤能量选择同一般的成人^[46],无需提高除颤能量。当孕妇出现心室纤颤(室颤)和无脉室性心动过速(室速)时可采取电除颤,双相波 120 ~ 200 J。除颤后不需要评估可立即进行 CPR,与非孕成人相同。因在除颤过程中只有相当小的能量传递给胎儿,因此在怀孕的任何阶段对患者进行除颤都是安全的。即便是正在使用胎儿监护仪,也不要因移除胎儿监护仪而延迟除颤^[59]。由于孕期呼吸系统的生理变化,孕妇的氧气储备有限,尤其注意患者血氧等情况,插管也应由最有经验的医生操作,使用内径 6.0 ~ 7.0 mm 的较小气管插管,以增加插管成功的可能性,同时避免反复插管失败导致孕妇及胎儿缺氧加重^[2]。

3.4.4 抢救用药: 孕期 CA 的抢救用药与非妊娠没有区别,如每 3 ~ 5 min 给予肾上腺素,对于顽固性室颤及室速推荐用胺碘酮,首剂 300 mg 后 150 mg 分次静脉注射(静注),阿托品不作为一线药物(心动过缓治疗除外)。无需顾忌妊娠及胎儿用药禁忌,使用剂量同非孕期成人^[60]。如果具有溶栓指征,可以考虑使用溶栓药物。

3.4.5 CPR 过程中胎儿监测: 复苏的目的是恢复孕妇的自主循环,过多强调评估胎儿心率不但没有帮助反而会耽误母体复苏的效果^[2, 60]。在 CPR 过程中,美国心脏协会(American Heart Association, AHA)指南建议无需对胎儿进行评估,所有的胎儿监护仪都应该从患者身上移除。CPR 的目的是恢复孕妇的血液循环,而此时评估胎儿心率不但没有帮助还会干扰对孕妇复苏的质量^[2]。

3.4.6 出血导致的 CA 处理: 一旦大出血,必须按照孕期大出血指南^[61-63],尽快成分输血或尽快将孕妇转送到可以输血的医院甚至监护室。一项大型的随机对照试验(randomized controlled trial, RCT)研究显示,静注氨甲环酸(1 g)尤其是在出血 3 h 内可以明显降低孕妇产后出血的死亡率^[64]。经皮冠脉介入成为孕妇 ST 段抬高型心肌梗死(ST segment

elevation myocardial infarction, STEMI)的再灌注治疗选择手段,溶栓治疗为紧急经皮冠脉介入治疗(percutaneous coronary intervention, PCI)不能提供情况下的重要治疗手段^[65]。一项 200 例高危 PE 的孕妇接受溶栓治疗的分析显示,孕产妇死亡率只有 1% 并显示溶栓治疗的安全性^[66]。

3.4.7 子痫前期和子痫处理: 子痫是指有子痫前期体征和症状的患者,在妊娠或产后发生惊厥和/或原因不明的昏迷、先兆子痫或者子痫抽搐。欧洲复苏委员会(European Resuscitation Council, ERC)建议遵循现有的子痫前期和子痫指南^[67]。

3.4.8 AFE: AFE 通常出现在分娩前后,伴有猝死、呼吸困难、紫绀、心律失常、低血压和与弥散性血管内凝血(disseminated intravascular coagulation, DIC)相关的出血。AFE 出现并在病情恶化之前可以有一些警示信号,包括呼吸困难、胸痛、感到寒冷、头晕、痛苦、恐慌、手指发麻、恶心和呕吐。英国产科监测系统(the UK Obstetric Surveillance System, UKOSS)在 2005 至 2014 年发现了 120 例 AFE,总发病率和死亡率分别约为 1.7/10 万和 0.3/10 万,并与高龄产妇、多胎妊娠、前置胎盘、引产、阴道器械分娩和剖宫产有关^[68]。AFE 治疗主要以支持治疗为主,相关治疗及复苏后的处理手段与其他手段相同,没有特异性治疗手段。目标温度控制已被安全有效地用于早期妊娠胎儿心脏监测,并有利于产妇的预后^[69-71]。

4 孕期预防 CA 的防治规范

研究发现 0.8% ~ 0.9% 的活产儿患有先天性^[72-73]。病变的严重程度不同,但即使是复杂病变的患者也能存活到生育年龄。一项关于怀孕与合并心脏病的国际多中心研究调查显示,2/3 孕妇患有心脏病^[74],5% 患有 PAH^[75-76]。欧美国家的研究显示先心病和 PAH 是罕见的产妇死亡原因^[17],我国的孕妇相关原因资料尚缺乏。其他如主动脉疾病、瓣膜病、结缔组织疾病等等,除了孕期特有的并发症外,上述疾病有时候很隐匿,可能在孕前诊断、也可以在孕时因为出现症状得以诊断。无论哪一种,处理原则基本相同,本节将孕期合并症和并发症的 CA 预防及治疗原则整合后一起推荐。

4.1 总体防治原则: 原则上不建议所有已知患有心脏或主动脉疾病的女性怀孕,并建议采取避孕措施。备孕或者一旦怀孕者,应尽快进行孕前咨询^[77]。为了进行风险评估,至少应该进行心电图、超声心动图和运动测试。主动脉病变者需要通过计算机

断层扫描(computed tomography, CT)或磁共振成像(magnetic resonance imaging, MRI)对完整主动脉成像及适当的孕前咨询。心率峰值和摄氧量峰值的监测可以帮助预测怀孕期间母亲的心脏事件、怀孕期间运动耐力与 80% 以上的妊娠良好结局^[78]。所有已知患有心脏或主动脉疾病的女性必须整体考虑以下几个方面的内容:长期预后、妊娠率和流产率、先天性疾病复发风险、药物治疗、估计产妇风险和结局、预期胎儿娩出以及妊娠护理和分娩计划。需要建立多学科管理计划,孕妇参与讨论并配合医生的整体管理。超重、吸烟和饮酒等不健康习惯会对孕产妇和胎儿产生不良的影响。并发症的风险可能会随着时间的推移而变化,风险评估需要在每次孕前检查时重新评估。患有心脏病的妇女于产前期与心衰有关^[79]。利钠肽水平与心脏事件的发生相关,妊娠 20 周时 N 末端脑钠肽前体(N-terminal pro-brain natriuretic peptide, NT-proBNP) >128 ng/L 可预测妊娠后期的事件^[80-81]。所有心脏病患者都应监测母体血压和心率。对于患有更严重心脏病的女性,动脉监测可以提供更准确的数据。建议脉搏血氧饱和度测量和持续心电监测,以发现失代偿的早期迹象及确定哪些患者应加快分娩。Swan-Ganz 导管与并发症相关,获益/风险尚不明确,不建议使用。

4.2 孕期用药:怀孕时的药代动力学会发生明显的生理变化(如心血管、肺及血液系统),可能会发生药物的吸收、分布、代谢和排泄等方面的改变^[26],突出体现在血浆容量、每搏量和心率增加;血浆胶体渗透压降低;凝血因子和纤维蛋白原增加;子宫对下腔静脉的压迫;潮气量和分钟通气量增加。肝细胞色素 P450 酶(如 CYP2D6、CYP3A4)的活性增加;恶心、呕吐及胃排空延迟;胃食管反流等。

4.2.1 抗凝药物:尽管低剂量华法林(<5 mg/d)相对安全,但是因其致胎儿畸形的风险限制了妊娠早期的使用。即便在妊娠中期和晚期使用华法林,也有 0.7%~2% 致胎儿畸形的风险(例如眼睛和中枢神经系统异常、颅内出血)^[82-85]。相对于华法林而言,现有指南推荐低分子肝素(low molecular weight heparin, LMWH),且与肝素比较,LMWH 导致的肝素相关的血小板减少症(heparin-induced thrombocytopenia, HIT)概率比较低^[86]。但与抗凝血酶Ⅲ(antithrombin Ⅲ, AT Ⅲ)结合间接抑制 Xa 因子活性的磺达肝羧酸钠,孕期的研究数据有限,曾有 65 例患者妊娠期使用磺达肝羧酸钠获得了良好结

果^[87],故建议对 LMWH 有明确的过敏或者不良反应者使用^[88]。利伐沙班因可以穿过胎盘,不建议用于孕期。其他的 Xa 因子抑制剂如阿哌沙班、艾多沙班、达比加群均不建议孕妇使用。

4.2.2 溶栓药物:溶栓药物在妊娠期和围产期被认为是相对禁忌证,只应在高危人群中使用。表现为严重低血压或休克患者出血的风险,生殖道出血最多见,约为 8%^[89]。溶栓药物包括重组组织型纤溶酶原激活剂(recombinant tissue plasminogen activator, rt-PA)和链激酶。两种溶栓药物都不会通过胎盘,但现有指南倾向于 rt-PA。具体使用方法与非孕期相同。于 2 h 内输注完 50 mg rt-PA 后继以普通肝素(unfractionated heparin, UFH) 18 U·kg⁻¹·h⁻¹ 开始输注,并维持活化部分凝血活酶时间(activated partial thromboplastin time, APTT)在正常范围的 1.5~2.5 倍,病情稳定后 UFH 可以切换到 LMWH^[90-91]。

4.2.3 心血管用药:β-肾上腺素能受体阻滞剂在妊娠期通常是安全的,但可能与胎儿生长受限率增加和低血糖有关。首选 β₁-受体选择性药物,其对宫缩和胎儿发育迟缓影响最小^[92];非选择性 β-受体阻滞剂如阿替洛尔,与较高的胎儿生长迟缓率有关^[92-93]。在 α/β 受体阻滞剂中,拉贝他洛是治疗妊娠高血压的首选药物,而最近发表的一项有 13 例患者接受卡维地洛治疗心衰的小型研究中未显示出与胎儿生长迟缓有任何关联^[92]。血管紧张素转换酶 I(angiotensin conversion enzyme I, ACE I)和血管紧张素Ⅱ受体拮抗剂(angiotensinⅡ receptor blocker, ARB)或者含有 ARB 的血管紧张素受体脑啡肽酶抑制剂(angiotensin receptor neprilysin inhibitor, ARNI)因有致畸性,为孕期禁忌证^[26]。在一项对 721 例妊娠晚期暴露于钙拮抗剂(calcium channel blocker, CCB)的研究中,报告了 CCB 增加新生儿癫痫发作的风险;地尔硫草在 36 429 只动物实验中证实具有致畸性,在人类中数据有限。同时建议只有在潜在的好处足以证明超过对胎儿的潜在风险时,才建议在怀孕期间使用维拉帕米,并被推荐为控制房颤速率和治疗孕妇特发性持续性房颤的二线药^[26]。他汀类药物不应在怀孕或哺乳期间用于治疗高脂血症,因为其无害性尚未得到证实。一项 249 例暴露于他汀类药物的胎儿的 RCT 研究中,出生缺陷率在病例组与对照组之间没有显著差异^[94]。孕妇不建议使用螺内酯,而托拉塞米或呋塞米可以使用^[26]。



4.2.4 介入治疗:如果干预是绝对必要的,孕第 4 个月为最佳时期,此时器官发生已经完成,胎儿甲状腺尚处于不活跃状态,子宫体积仍然较小,因此胎儿与胸部之间的距离比后期更大。妊娠期 STEMI 的治疗主要依赖于 PCI。应遵循“合理可达到的低剂量”原则。减少辐射的措施有:① 尽可能使用超声引导。② 将放射源尽可能远离患者,而将接受器尽可能靠近患者。③ 仅使用低剂量透视。④ 倾向于前后投影。⑤ 避免腹部的直接辐射。⑥ 尽量聚焦可能发生病变的区域。⑦ 尽量缩短透视时间。⑧ 配合有经验的心脏病专家^[95-96]。腹部屏蔽在一定程度上降低了胎儿的辐射剂量,监测和记录辐射照射有助于日后评估对胎儿可能产生的影响。UFH 必须以 40~70 U/kg 静注,目标是激活的凝血时间为 250 s (200~300 s)或 APTT 处于正常范围的 1.5~2.5 倍。

4.2.5 体外循环:体外循环期间的产妇死亡率与非孕妇的死亡率相似;然而,胎儿死亡率仍然很高(达 20%)^[97]。通过对母体和胎儿的严密监测,可以将对母体和胎儿的风险降至最低。胎龄对新生儿结局有很大影响^[98-99]。如果胎龄>26 周,可以考虑在体外循环前剖腹产^[97]。在体外循环过程中,应该监测胎儿心率和子宫张力,为了胎儿结局更好,应该尽量缩短体外循环时间^[100-101]。对于计划剖腹产的妇女,抗凝期间的分娩(非机械瓣膜),可以在手术前 24 h 停用治疗性 LMWH。如果分娩必须更早进行,使用抗 Xa 活性监测指导手术的时间。在高危妇女,治疗性 UFH 可在产后 6 h 重新开始。对于中危或低危的妇女,可以在产后 6 h 给予单剂量的 LMWH 预防,12 h 后重新开始治疗性 LMWH,例如,依诺肝素 20 mg (体重<50 kg)、40 mg (体重 50~90 kg)、0.5 mg/kg (体重>90 kg)。如果计划阴道分娩,可将中高患者转为输注 UFH,同时定期检查 APTT 以优化控制,并在插入区域麻醉或预期分娩前至少 4~6 h 停止输注。对于低风险的妇女,可在预产期前 24 h 内暂停治疗性 LMWH。恢复抗凝可按上述方法重新启动。

4.2.6 抗凝治疗下的紧急分娩:在 LMWH 的情况下,应给予鱼精蛋白中和。然而,孕期不仅抗 Xa 因子活性持续延长,出血倾向持续存在^[102],而且皮下注射后 LMWH 的半衰期更长,吸收时间更长,因此可能需要重复剂量或输注硫酸鱼精蛋白。如果患者使用口服抗凝药物(oral anticoagulant, OAC),首选剖腹产以减少胎儿颅内出血的风险。4 因子凝血酶

原复合物浓缩物即凝血因子 II (凝血酶原)、VII (促凝血酶原激酶原)、IX (抗血友病球蛋白 B)、X (自体凝血酶原 C)组成的复合物浓缩物的抗凝逆转效果较好。建议根据产妇体重、初始国际标准化比值(international normalized ratio, INR)和目标 INR 给予^[103],优于新鲜冷冻血浆(12~15 mL/kg)^[104],应在剖宫产前给予,以达到 INR≤1.5。必要时给予维生素 K (5~10 mg 静注),但可能需要 8~12 h 才能逆转 INR,并具有持久的效果,使再抗凝更加困难。产妇停用 OAC 后,胎儿仍可保持抗凝状态约 8~10 d,可能需要给予新鲜冷冻血浆和维生素 K。

4.3 孕期检查:怀孕期间发生的生理变化,对及早诊断心衰会增加一定的难度。当发生不成比例的或无法解释的气促、呼吸困难或者体检闻及新出现的病理性杂音时,需要及时进行相关的客观检查,如超声心动图检查,并建议有在心血管疾病诊断领域足够经验的医生参与诊断。

4.3.1 心电图:绝大多数孕妇,心脏向左旋转,心电图显示电轴左偏约 15°~20°。常见的其他改变包括 ST/T 波改变,导联 III 的 Q 波和倒置 T 波,导联 aVF 的递减 Q 波, V1、V2 和偶发 V3 的倒置 T 波。上述改变可能与左室肥厚和其他结构性心脏病类似。已知既往有阵发性/持续性心律失常如室速、房颤或心房扑动或报告有心悸的患者应进行动态心电图监测。

4.3.2 超声心动图:经胸超声心动图是妊娠期首选的影像学检查方法。这种可重复、无创、便捷的诊断方式可以在门诊和心脏科病房、急诊科、重症监护病房(intensive care unit, ICU)或产科病房使用。妊娠期间,波形参数可能会发生一些变化,如腔室轻度扩张、左室壁厚度变化和瓣膜梯度增加。经食管超声心动图相对安全;然而,应考虑呕吐/误吸和腹内压突然升高的风险,并进行胎儿监护^[24, 105]。

4.3.3 运动测试:生理运动测试是成人先心病和瓣膜病随访的重要组成部分^[36, 106],应在已知心脏病并计划怀孕的患者中进行。尚无证明已怀孕的疑似心脏病的无症状患者进行最大运动测试(预测最大心率的 80%)会增加自然流产的风险^[37]。采用运动试验进行超声心动图监测可提高诊断的特异性^[107]。由于怀孕本身就是一种应激状态,孕期很少出现多巴酚丁胺应激,应避免使用多巴酚丁胺。

4.3.4 电离辐射:照射对胎儿潜在的危险取决于怀孕阶段和吸收剂量,其在器官发生期和胎儿早期

风险最高,中期风险较小,晚期风险最小^[108]。畸形通常与中枢神经系统有关。在妊娠早期(包括植入前 0~8 d),辐射剂量>250 mGy 会导致自然流产;100~200 mGy 会出现生长限制、智力残疾、恶性肿瘤和神经系统影响^[109-110]。最脆弱的时期包括 8~56 d 的生长迟缓,14~105 d 的小头畸形,56~105 d 的智力缺陷、癫痫发作、严重智力障碍^[111]。据报道,宫内辐射剂量约为 20 mGy 时,儿童患癌症的风险增加,每 3 000 名宫内暴露于 10 mGy 辐射的儿童中,约有 1~2 例儿童出现癌症^[112]。所有医疗辐射剂量必须保持“尽可能低”,充分告知母亲医疗辐射相关的风险,并获得知情同意。

4.3.5 胸部 X 线和 CT 扫描:怀孕期间的的心脏疾病,胸部 CT 通常是不必要的,也不推荐,除非在其他诊断工具不足的情况下诊断或排除 PE 或主动脉病变,以及可以使用 0.01~0.66 mGy 的低辐射 CT^[106, 113]。

4.3.6 心导管:心导管检查很少以诊断为目的,多用于指导介入治疗。未屏蔽腹部的平均辐射暴露为 1.5 mGy,其中不到 20% 到达胎儿。有研究辐射剂量分别为 260、58 和 19 cGy/cm² 时,子宫(胎儿)预计可能接受的辐射剂量分别小于 0.005、0.001 和 0.000 5 mGy^[114]。建议由有经验的操作员进行径向入路,并采用电解剖测绘系统以减少辐射剂量。

4.3.7 核磁:如果其他非侵入性诊断方法不足以明确诊断,建议使用 MRI,如果可能,建议使用基于电离辐射的成像方法^[106, 108]。妊娠期使用钆造影剂的证据存在争议,尽可能避免使用,特别是在妊娠早期。基于现有的研究显示,给药后继续母乳喂养是安全的,钆的制剂经过母乳的排泄是有限的:最初 24 h 内<0.04% 的静脉剂量大概有 1%~2% 被吸收^[115]。

4.3.8 基因检测:与没有心血管疾病的父母相比,遗传心脏缺陷的风险显著增加(约为 1%)^[72, 116]。遗传率在 3%~50%,取决于父母心脏病的类型。父母有常染色体显性疾病如马凡综合征、肥厚性心肌病(hypertrophic cardiomyopathy, HCM)或长 QT 综合征(long QT syndrome, LQTS)的孩子有 50% 的遗传风险。最终的表型也将由不完全外显和多效性的效应决定,并且可能有显著差异。对于以多基因方式遗传的缺陷,复发风险定义尚未明确。心肌病的基因检测不适用于扩张性心肌病(dilated cardiomyopathy, DCM)的产前诊断,除非经过详细的临床和家庭评估后,在专家团队的设置下选定疾病或高危情况^[117]。在静脉血栓栓塞症(venous

thrombosis embolism, VTE)患者中,基因检测被认为对缺乏天然抗凝剂或复发性 VTE 患者的亲属是合理的^[118]。对于重大先心病,12 周超声检查的敏感性和特异性分别为 85% 和 99%,颈襞厚度正常的先心病发生率约为 1/1 000^[119]。重大畸形的早期诊断使父母可考虑所有选择,包括终止妊娠^[120]。所有患有先心病的妇女都应在妊娠 19~22 周进行胎儿超声心动图检查,45% 的先天性心脏畸形已被发现^[121-122]。胎儿超声心动图应由有经验的专家进行^[121-123]。

4.4 孕期特殊疾病的治疗

4.4.1 PAH:2022 年欧洲心脏病学会(European Society of Cardiology, ESC)/ERC 更新了 PAH 的定义:右心导管监测平均动脉压 ≥ 20 mmHg(1 mmHg ≈ 0.133 kPa),肺血管阻力 ≥ 2 wood unit,毛细血管楔压(pulmonary arterial wedge pressure, PAWP) ≤ 15 mmHg^[124]。未经治疗的 PAH 患者的中位生存期为 2.8 年,常见于女性,往往其临床表现在妊娠期被识别^[125]。PAH 患者的管理贯穿孕期、产时及产后,需要有经验的产科团队及肺循环专家团队的多学科联合救治及远期的系统追踪和治疗对策的调整^[126]。

4.4.2 主动脉疾病:具有遗传性特征的胸主动脉疾病很容易形成动脉瘤和 AD。这些包括遗传性胸主动脉疾病(heritable thoracic aortic disease, HTAD)及其综合群(马凡综合征、Loeys-Dietz 综合征、Osteoneurysm 综合征和 Vascular Ehlers-Danlos 综合征)或非 HTAD(即仅有主动脉瘤)。其他形式的先心病,如法洛四联症和主动脉狭窄(coarctation of the aorta, CoA)也可伴有主动脉扩张,最终可能发生非遗传性主动脉病变。高血压和高龄产妇成为主动脉扩张的重要危险因素^[127]。对于所有患有主动脉病变的患者来说,妊娠期处于高危期,尽管妊娠期很罕见,但与极高的死亡率密切相关^[128-129],且大多数死亡无明确的主动脉疾病病史。基于这部分女性患者中大多数患有遗传性疾病,因此建议尸检,进行 DNA 分析作为下一步进行家族史筛查的重要依据^[130-131]。怀孕期间的血流动力学和激素变化增加了 AD 的易感性^[132]。剥离最常发生在妊娠最后 3 个月(50%)或产后早期(33%)。所有已有遗传相关的研究证明,主动脉疾病或家族性主动脉疾病病史的妇女都应该接受有关 AD 风险和复发风险的咨询,并在怀孕前进行包括整个主动脉成像在内的完整评估。在评估主动脉直径时,应考虑体表面积,特别是



在身材矮小的女性。异位似乎与主动脉直径增加有关^[133]。孕期主动脉扩张具体情况尚不清楚^[134]。所有孕期出现胸痛的患者,都应考虑 AD 的可能。马凡综合征妇女发生与怀孕相关的 AD 的总风险为 3%^[135]。主动脉根部的宽度是风险的主要决定因素,主动脉根 >45 mm 的女性会增加夹层的风险;当主动脉为 40~45 mm 时,需要考虑其他因素,如 AD 家族史及主动脉生长速率等^[130]。主动脉弓部置换后仍会面临着主动脉远端剥离和其他血管剥离^[136]。但是马凡综合征患者妊娠期潜在生长速率的研究结果恰好与此相反。有些表现为无明显生长,而另一些则生长 ≥ 3 mm,但产后部分直径减小^[134, 137]。产科并发症也增加了胎膜早破的概率^[138]。发生在怀孕期间的 Stanford A 型 AD 属于外科急症,需要经验丰富的心胸外科、心脏病学、产科和心脏麻醉等多学科共同合作。同时,如果胎儿娩出无法存活,建议在胎儿存在的情况下进行主动脉手术。如果胎儿分娩后可以存活,可以在剖宫产的同时进行 AD 的修复,这种情况下虽然产妇结局良好,但胎儿死亡率高达 20%~30%^[139]。对于无并发症的 B 型 AD,建议在妊娠期间保守治疗,药物严格控制血压即可^[140]。升主动脉直径为 40~45 mm 时,应考虑阴道给药并加快二期及局部麻醉,以防止血压升高,避免剥离。根据产妇个人情况,也可以考虑对这些患者进行剖腹产。建议当主动脉直径 >45 mm、存在血管 Ehlers-Danlos 综合征 IV 型或急性、慢性 AD 患者应行剖宫产。

4.4.3 瓣膜病:二尖瓣病变患者约 50% 会发生主动脉扩张,即使在瓣膜功能正常情况下也会发生主动脉扩张,且当发生在升主动脉远端,超声心动图不容易识别,极易漏诊,应在怀孕前进行 MRI 或 CT 检查以最大化降低剥离的风险。二尖瓣病变患者发生主动脉扩张的危险因素基于二尖瓣的类型、形态、主动脉扩张和 CoA^[141]。当主动脉内径 >50 mm 时应避免妊娠。严重的血管并发症几乎只发生在 IV 型 Ehlers-Danlos 综合征(血管型)。产妇死亡率很高,与子宫破裂、大动脉和静脉夹层有关。怀孕被认为是一种高风险行为,不建议这类女性怀孕或应该共同参与决策^[142]。Turner 综合征与先天性疾病的风险增加有关,如心脏病、主动脉扩张、高血压、糖尿病和动脉粥样硬化等事件^[143]。Turner 综合征很少发生 AD,但在年轻人中,其发病率是成年人的 6 倍^[144-145]。AD 的危险因素包括主动脉扩张、二尖

瓣病变及 CoA^[146]。当主动脉指数 >25 mm/m² 应避免怀孕。主动脉瓣手术后,患者仍有发生 B 型 AD 的风险。良好的血压控制和糖尿病对 Turner 综合征患者孕期管理是必要的^[143]。

4.4.4 冠心病:育龄妇女 CAD 的发病率尚不清楚,各国的情况各不相同。尽管 AMI/ACS 合并妊娠相对少见(1.7/10 万~6.2/10 万分娩)^[147-149],CAD 占所有孕产妇心脏死亡的 20%^[17]。与同龄的非孕女性相比,怀孕时 AMI 风险增加 3~4 倍。相关危险因素包括吸烟、年龄、高血压、糖尿病、肥胖和血脂异常^[150-151];其他危险因素包括先兆子痫、血栓形成、输血、产后感染、可卡因的使用、多胎和产后出血^[148]。随着 40 岁以下妇女生育率的增加,ACS 合并妊娠将变得更加常见,因为产妇年龄每增加 1 岁,AMI 的风险就增加 20%^[149]。妊娠期冠心病的病因与一般人群不同;大多数 CAD 具有非动脉粥样硬化机制,包括妊娠相关的自发性冠状动脉夹层(pregnancy-related spontaneous coronary artery dissection, P-SCAD, 43%)、冠状动脉(冠脉)造影正常(18%)和冠脉血栓形成(17%)^[151-152]。与 P-SCAD 相关的 AMI 最常发生在妊娠晚期/产后早期,主要累及左侧冠脉,常累及多支血管^[151]。与妊娠相关的潜在诱发因素包括导致冠脉血管结构改变的雌激素/孕酮水平的波动,纤维肌发育不良或结缔组织疾病的背景以及与分娩相关的冠脉剪切应力的增加^[153-155]。冠脉造影正常的 AMI 的发病机制尚不清楚,包括短暂的冠脉痉挛(血管反应性增加和/或使用麦角衍生物)^[156]。无动脉粥样硬化的冠脉血栓形成最可能是由于妊娠期的高凝性^[157],也可能是矛盾栓塞的结果。川崎病生存率的增加(在美国,预计到 2030 年,每 1 600 名成年人中将有 1 人患有川崎病)带来了额外的挑战^[158]。川崎病的相关表现包括动脉瘤、冠脉血流改变、冠脉狭窄、心肌缺血/纤维化、充血性心衰和瓣膜异常。妊娠相关 ACS/AMI 的发展最常见的是在妊娠晚期[STEMI 25%,非 STEMI (NSTEMI)32%]或产后(STEMI 45%,NSTEMI 55%)。临床表现与非妊娠人群相同^[159-160]。心电图解释可能是具有挑战性的,在没有冠脉缺血的情况下出现倒置 T 波、剖腹产麻醉诱导可能会出现 ST 段压低。在心电图不能确诊的情况下,超声心动图可以协助鉴别诊断,包括 PE、AD 和先兆子痫^[161]。潜在并发症包括心衰/心源性休克(38%)、心律失常(12%)、复发性心绞痛/AMI(20%)、孕产妇死亡率(7%)和

胎儿死亡(7%)^[151]。妊娠期 AMI 的处理与一般人群相似,包括血运重建技术。在 P-SCAD 中,应用血管重建策略时应考虑血管脆性的增强^[162]。管理应该是多学科的,包括急诊、产科和心血管团队,任何血运重建都应该由最有经验的操作员进行,因为在这一患者群体中有冠脉介入的伴随风险。在心源性休克中,应该有紧急机械循环支持设施。需要对母体和胎儿进行密切监测,并制定分娩策略,以防母体或胎儿突然恶化。如果产妇 CA,应根据现有指南进行复苏和分娩。关于指南推荐的 AMI 药物治疗的胎儿安全性的数据很少^[163]。低剂量阿司匹林相对安全, P2Y₁₂ 受体抑制剂的信息很少。氯吡格雷应仅在严格必要时使用,且使用时间尽可能短^[151]。在没有糖蛋白 II b/III a 抑制剂(如比伐瑞丁、普拉格雷和替格瑞洛)的使用证据的前提下,不建议使用。PCI 术中短期肝素化的好处可能超过出血并发症的风险。电离辐射的影响不应阻止 AMI 血管重建标准指征的妊娠患者的原发性 PCI。但是,辐射剂量必须最小化,对于稳定、低风险的 NSTEMI,应考虑采用非侵入性方法^[164]。尽管 CT 冠状动脉造影术提供了一种替代的诊断方法,它需要放疗和潜在的高剂量 β -受体阻滞剂,且不能显示有限的 P-SCAD。大多数关于妊娠期 STEMI 的报道都与裸金属支架有关。然而,根据 2017 年 AMI STEMI 指南推荐新一代药物洗脱支架(drug eluting stent, DES)。有冠心病或 ACS/AMI 的妇女在怀孕期间有严重不良心脏事件的风险,其中最高的风险是动脉粥样硬化性 CAD^[160, 165],死亡率在 0%~23%^[75, 166-167]。不良产科结局发生率 $\leq 16\%$, 30% 的妊娠并发不良胎儿/新生儿事件,最常见的是冠脉粥样硬化(50%)^[165]。已知 CAD 患者如果无残余缺血和左室功能障碍的临床体征,则可考虑妊娠。没有高质量的数据来定义 AMI/ACS 后怀孕应该推迟多长时间,建议 12 个月似乎是合理的,根据合并症、心血管状况和药物治疗的需求,个性化治疗。没有确切证据表明既往 P-SCAD 会增加复发风险,然而,建议避免进一步怀孕^[164],如果患者选择继续怀孕,建议密切监测。分娩时间必须因人而异, STEMI/NSTEMI 的治疗不应因分娩而延误。AMI 后,如果可能,应将分娩推迟至少 2 周,以方便产妇管理^[168],阴道分娩为佳。

4.4.5 心肌病、心衰及其管理:妊娠相关心肌病的病因包括获得性和遗传性两种,如 PPCM、中毒性心肌病、HCM、DCM、Takotsubo 心肌病等。虽然罕见,

但可能导致严重的妊娠并发症^[169]。PPCM 重要的易患因素包括多胎、非洲裔、吸烟、糖尿病、先兆子痫、营养不良、高龄和少女怀孕^[170-171]。具体病因尚不明确,可能的病因包括炎症和血管生成失衡,导致血管损伤^[172]。PPCM 的诊断表现为继发于妊娠末期和产后数月的左室收缩功能障碍的心衰,大多数诊断为产后,同时借助于准确的既往病史,以确定和排除心衰的其他原因^[173]。左室可无扩张,但左室射血分数(left ventricular ejection fraction, LVEF)通常 <0.45 。患者通常表现为典型的急性心衰,部分存在室性心律失常和/或 CA。超声心动图是首选的成像方式。初始 LVEF <0.30 标志着左室扩张(左室舒张期末直径 ≥ 6.0 cm),右室受累通常会与不良结局相关。急性/亚急性心衰和心源性休克可在妊娠期或妊娠后迅速发展,一旦发生在应用血管收缩性药物或血管加压药时,尽早转移到有机械循环辅助设施的医院。紧急剖腹产分娩(无论妊娠与否)应考虑立即提供机械循环支持。PPCM 患者对 β -肾上腺素能激动剂的毒性作用敏感,应尽可能避免^[174-175]。左西孟旦可能是首选的收缩剂^[176-177]。应对既往有心肌病的孕妇进行评估。鉴别诊断包括有无并发症、妊娠、肺水肿(子痫前期/子痫)、PE、肺炎和心肌梗死^[178]。治疗目标与非妊娠期急性心衰相似,同时避免使用胎儿毒性药物(ACE I、ARB、ARNI 和阿替洛尔)。合并肺充血的心衰患者,如有需要,可使用袢利尿剂和噻嗪类药物治疗。在没有肺淤血的前提下,尽可能避免使用利尿剂,以防出现潜在的胎盘血流量减少^[179]。有关妊娠期肼拉嗪和硝酸盐等药物带来的益处证据少于 ACE I,但现有指南推荐在高血压、严重左室功能障碍和/或失代偿性心衰中使用相对安全。慎用 β -受体阻滞剂,基于高静息心率是 PPCM 不良结局的预测因子,必要时使用应逐渐加量至靶剂量^[170, 180]。PPCM 和 DCM 的标准抗凝主要适用于妊娠期间和产后。抗凝剂的选择取决于妊娠阶段和患者偏好^[4, 181]。对于 LVEF 下降的 PPCM 患者,应考虑预防性抗凝^[169]。晚期心衰且血流动力学不稳定的妇女,无论妊娠期长短,都应考虑紧急分娩。为了防止压力或容量突然变化,硬膜外麻醉可能是剖腹产后一种选择的方法,但应在麻醉专家的指导下进行^[174, 179]。稳定的充血性心衰患者,首选阴道分娩。对于 LVEF 降低的心衰患者,尤其是纽约心脏病协会(New York Heart Association, NYHA)心功能 III/IV 级时,不建议母乳



喂养,尽可能减少泌乳导致的高代谢需求,尽快促进母亲的心功能恢复。关于母乳喂养期间的药物治疗,产后规律专科门诊动态评估。如果已经在服用 β -受体阻滞剂,应该继续服用。当出现新的症状时,应开始使用维拉帕米,控制房颤的速率,抑制室性心律失常。当不能耐受 β -受体阻滞剂时,维拉帕米作为第二选择(因胎儿监测有导致房室传导阻滞的可能)^[182-183]。对于耐受不良的持续性房颤,应考虑复律治疗^[181]。对于阵发性或持续性心律失常,建议采用抗凝治疗。有猝死史或猝死家族史的患者,如果出现心悸或晕厥前驱症状,应密切监测并及时调查。必要时应植入装置确保安全^[184]。低风险病例可以自然分娩,对于重度左室流出道梗阻、OAC 时早产或严重心衰的患者应考虑剖宫产^[4]。

4.4.6 心律失常:快速心律失常中,房颤可成为首发症状,并在妊娠期间发作更加频繁^[185-186],尤其是患有先心病的女性^[187-188]。房颤(27/10 万)和阵发性室上性心动过速(paroxysmal ventricular tachycardia, PSVT, 22~24/10 万)是除期前收缩(早搏)外最常见的心律失常^[185]。PSVT 的症状加重通常是良性的,可以通过药物有效治疗^[189-190]。危及生命的室颤、慢性心律失常在怀孕期间是非常罕见的。房颤和快速的室性心律失常与死亡风险的增加密切相关^[185],如已知有任何症状性室上性心动过速(supraventricular tachycardia, SVT)或室速病史的患者应考虑在怀孕前进行导管消融。患有先天性 LQTS 的妇女在产后期间发生心脏事件的风险非常大,新发室速应排除潜在的与母亲 SCD 风险增加相关的结构性心脏病^[185, 191]。PSVT 患者的产科和胎儿的结局都比较差,在严重产妇、剖宫产、低出生体重、早产、胎儿压力和胎儿畸形方面的发生率均高于无 PSVT 患者^[192]。患有先心病的妇女在分娩时比未患先心病的妇女更容易死亡,心律失常是最常见的心血管事件^[188]。当持续的房颤是血流动力学不稳定或者对母亲或胎儿有相当大的风险时,建议电转复^[181]。对于心脏结构正常的稳定患者,可考虑静脉输注布利特或弗莱卡因来终止心房扑动(房扑)和房颤^[190, 193]。转复前一般应进行抗凝治疗,首选静注 β -受体阻滞剂控制心率。在采用心率控制策略的情况下,推荐使用口服 β -受体阻滞剂。先心病患者的房扑建议用电转复以恢复窦性节律。当心功能受损,慎用 β -受体阻滞剂、I 类抗心律失常药物和索他洛尔(Sotalol)。预防卒中风险分层,抗

凝治疗应用原则与非妊娠患者相同。怀孕期间禁止服用华法林^[181]。在怀孕期间或怀孕后,应始终通过适当的诊断试验寻找遗传性心律失常^[194]。如果在妊娠最后 6 周或产后早期出现新发室速,应排除 PPCM^[170]。如果在怀孕期间出现指征,建议植入心脏复律除颤器(implantable cardioverter defibrillator, ICD)。考虑到分娩后自发性恢复率相对较高(50%),对于室速或 LVEF 较低的 PPCM 患者,ICD 的植入应遵循 ESC 指南^[194]。对于先天性 LQTS 患者^[195]和多型性室速患者^[196],非选择性 β -受体阻滞剂应在整个妊娠期和产后(产后至少 40 周)持续使用。对于先前无晕厥、尖端扭转(TdP)或任何其他风险特征的 LQTS 患者,可以使用选择性 β -受体阻滞剂^[2]。孤立性先天性高度房室传导阻滞在妊娠期对母亲预后影响不大。对于高度房室传导阻滞的稳定患者,分娩期间无需安装临时起搏器,但推荐在有心动过缓和晕厥风险的特定症状妇女中使用^[197-198]。导管消融应尽可能推迟到妊娠中期,并在有经验的中心进行^[199-200]。对于有 SCD 高危因素的患者,应在怀孕前考虑植入 ICD^[194]。ICD 植入过程中关于辐射的安全考虑与导管消融的讨论相似。皮下 ICD 因可能会出现起搏异常及较高比例的休克发生风险,可能导致分娩过程中 ICD 失活。建议在分娩前进行常规的 ICD 询问和建议。植入 ICD 最好是单腔^[201],特别是如果胎儿超过 8 周妊娠。超声心动图引导或电解剖标测会有很大帮助^[202]。

4.4.7 高血压急症:妊娠期高血压疾病是最常见的并发症,仍然是孕产妇、胎儿和新生儿发病及死亡的主要原因。产妇的风险包括胎盘早剥、卒中、多器官衰竭和 DIC。胎儿可能面临着宫内生长迟缓(25% 子痫前期)、早产(27% 子痫前期)和宫内死亡(4% 子痫前期)的高危状态。严密监测血压,重度高血压定义为间隔 ≥ 15 min,血压 $\geq 160/110$ mmHg,妊娠期高血压的定义仅基于在医疗机构的收缩压(systolic pressure, SBP) ≥ 140 mmHg 和 / 或 舒张压(diastolic pressure, DBP) ≥ 90 mmHg^[201, 203-204],并区分轻度(140~159/90~109 mmHg)或严重($\geq 160/110$ mmHg)血压升高,与 ESC/ESH 高血压联合指南所使用的分级不同^[205]。妊娠期高血压不是一个单一的实体,包括^[4]: ① 预先存在的高血压:妊娠前或妊娠 20 周前发生。通常持续产后 42 d 以上,可能与蛋白尿有关。② 妊娠高血压:妊娠 20 周后出现,通常在产后 42 d 内缓解。③ 先兆子痫:妊

妊娠高血压伴明显蛋白尿[$>0.3\text{ g}/24\text{ h}$ 或尿微量白蛋白/肌酐比值(albuminuria/creatinine ratio, ACR) $\geq 30\text{ mg}/\text{mmol}$]。妊娠期高血压多见于首次妊娠、多胎妊娠、葡萄胎、抗磷脂综合征、高血压、肾病或糖尿病的患者。胎盘发育不足导致的胎儿生长受限是早产的常见原因,唯一的治疗方法是分娩^[206]。蛋白尿可能是子痫前期的晚期表现,当发生高血压伴有头痛、视力障碍、腹痛或实验室检查异常(特别是血小板低和/或肝功能异常)时,应怀疑为子痫前期。④ 已有高血压,合并妊娠期高血压伴蛋白尿。⑤ 产前不可分类的高血压,主要是指妊娠 20 周后首次记录血压并诊断为高血压,需要产后 42 d 后重新评估。在第 12 周到 36~37 周期间,建议有较高或中度子痫前期风险的女性每天服用 100~150 mg 的阿司匹林。先兆子痫的高风险包括以下任意一种:① 先前怀孕期间的高血压疾病。② 慢性肾病。③ 自身免疫性疾病,如系统性红斑狼疮或抗磷脂综合征。④ 1 型或 2 型糖尿病。⑤ 慢性高血压。子痫前期的中风险包括以下危险因素中 1 种以上:① 首次怀孕。② 年龄 ≥ 40 岁。③ 怀孕间隔超过 10 年。④ 第一次就诊时体重指数(body mass index, BMI) $\geq 35\text{ kg}/\text{m}^2$ 。⑤ 子痫前期家族史。⑥ 多胎妊娠。对于膳食钙摄入量低($<600\text{ mg}/\text{d}$)的妇女,建议在第一次产前诊断开始补充钙(1.5~2.0 g/d,口服)以预防先兆子痫。维生素 C 和维生素 E 不能降低子痫前期风险;相反,会与出生体重 $<2.5\text{ kg}$ 和不良围产期结局相关^[207-208]。目前尚缺乏关于妊娠期高血压治疗的循证医学数据,相关研究中,严格控制和不严格控制妊娠期高血压与较轻度的孕产妇高血压相关,但在不良围产期结局的风险和总体严重的孕产妇并发症方面无差异^[209]。然而,数据的二次分析显示,患有严重高血压的妇女有较高的产妇不良事件发生(子痫前期、血小板 $<100\times 10^9/\text{L}$ 、有症状的肝酶升高、产妇住院时间 $\geq 10\text{ d}$)和围产期结局(围产期死亡、 $>48\text{ h}$ 高水平新生儿护理、出生体重小于正常体重的 10%、子痫前期和早产)^[207]。因此,目前没有证据支持妊娠期血压目标值。妊娠期高血压的非药物治疗作用有限,随机研究显示饮食和生活方式干预对妊娠结局的影响极小。应谨慎地继续进行定期锻炼,建议肥胖妇女(BMI $\geq 30\text{ kg}/\text{m}^2$),避免体重增加超过 6.8 kg^[210]。严重高血压的定义没有统一的标准,其范围在 160~180 mmHg 到 110 mmHg 之间。孕妇 SBP $\geq 170\text{ mmHg}$ 或 DBP $\geq 110\text{ mmHg}$ 为

紧急情况,需要住院治疗。降压药的选择和给药途径取决于预期给药时间。禁用 ACE I、ARB 和直接肾素抑制剂。应开始静注拉贝他洛尔、口服甲基多巴或奈夫地平治疗;静注肼丙嗪已不再是首选药物;肼丙嗪或静注乌拉地尔为常用的降压药,其次为硝普钠^[211]。当先兆子痫合并肺水肿时,首选药物是硝酸甘油静脉滴注 5 $\mu\text{g}/\text{min}$,每 3~5 min 逐渐增加至 100 $\mu\text{g}/\text{min}$ 。尽管缺乏证据,但欧洲指南^[4, 205, 212]建议所有血压持续升高 $\geq 150/95\text{ mmHg}$ 和血压 $>140/90\text{ mmHg}$ 的女性伴有下列任意一个症状时开始药物治疗:① 妊娠期高血压(伴或不伴蛋白尿)。② 高血压合并妊娠期高血压。③ 妊娠期任何时间出现亚临床器官损伤或症状性高血压。首选甲基多巴、 β -受体阻滞剂(如拉贝他洛)和钙拮抗剂(如硝苯地平)^[213-214]。子痫前期血浆容量减少,除非在少尿的情况下,才可以考虑使用小剂量呋塞米。推荐静注硫酸镁用于预防子痫和治疗癫痫,但由于潜在的协同作用,存在低血压的风险,不应与 CCB 同时使用^[215]。

4.4.8 孕期 VTE 的管理: 流行病学和产妇 VTE 的风险,包括 PE 和深静脉血栓形成(deep venous thromboembolism, DVT),是妊娠相关高死亡率的一个重要原因。妊娠期和产褥期 VTE、PE 发生率分别为 0.05%~0.20%^[216-217] 和 0.03%^[218-219]。英国资料显示每 10 万例妊娠中有 1.26 例 PE 患者死亡,为孕产妇死亡的第五大原因^[17]。VTE 的风险在产后初期最高,发生率约为 0.5%,产后第 6 周后恢复到非妊娠水平^[218, 220]。既往患有 VTE 者孕期复发率为 7.6%。并且即便使用了 LMWH,高危人群的复发率仍为 5.5%。妊娠相关静脉血栓的危险因素只要具有 1 个,VTE 的发生率就会从 0.02% 增加到 0.05%^[220-221]。因此,所有妇女都应该在怀孕前或怀孕早期接受 VTE 危险因素的系统评估,将妇女分为 VTE 的高、中、低风险人群,并采取相应的预防措施^[222]。前瞻性的非随机研究表明,在有危险因素的妇女中,VTE 的复发率为 2.4%~12.2%;而在接受抗凝治疗的妇女中,VTE 的复发率为 0%~5.5%^[223-224]。LMWH 已成为预防和治疗妊娠患者 VTE 的首选药物,尽管 LMWH 导致骨质流失比 UFH 少见,但因骨质疏松导致的孕妇骨折发生率为 0.04%^[86],建议用于血栓预防 LMWH 的初始剂量应基于孕前体重(或第一次产检体重)。建议每天接受一次 0.5 U/kg 的预防性依诺肝素或另一种同等剂量的 LMWH。在病态



肥胖的女性中,为了达到足够的抗 Xa 浓度,以体重为基础的给药比固定给药更合适^[225-226]。

妊娠期 PE 的症状和体征与非妊娠期相同(呼吸困难、胸痛、心动过速、咯血和虚脱)。然而,由于呼吸困难和心动过速在正常妊娠中较为常见,提高警惕并进行客观检测有助于及早诊断,单纯依据孕期 PE 的主观临床评价较为困难。非孕期 VTE 的临床预测规则如 D-二聚体(D-Dimer)检测、加压超声在孕期 VTE 诊断存在诸多局限,必要的低剂量 CT 肺血管造影或肺通气/灌注扫描可以确诊^[91]。研究显示,孕期 D-Dimer 水平平均为 (0.43 ± 0.49) mg/L,在第一、第二和第三个妊娠期分别上升到 (0.58 ± 0.36) 、 (0.83 ± 0.46) 和 (1.16 ± 0.57) mg/L,妊娠期 D-Dimer 水平相对增加 39%。妊娠期 D-Dimer 检测呈阳性并不一定意味着 VTE,需要进一步的客观检测。D-Dimer 检测阴性有助于排除妊娠 VTE。但据报道,在患有 VTE 的孕妇中 D-Dimer 水平可以正常,必要的影像学检查仍是诊断的重要方法^[227-229]。对疑似 PE 的孕妇,改良 Wells 评分或者联合 D-Dimer 检测可以合理地选择出必要的肺动脉血管造影术(computed tomography pulmonary angiography, CTPA)或者肺灌注检查人群,以避免不必要的辐射暴露^[230-232]。如果 DVT 可能性极高,加压超声作为首选。如果呈阴性,则需要进一步检查并进行 MRI 检查。如果怀疑有 PE 且其他检查均正常,则应进行低剂量 CTPA 检查。LMWH 已成为治疗妊娠期和产褥期 VTE 的首选药物。疑似 DVT 或 PE 时,应给予治疗性剂量 LMWH,直到客观检测排除诊断;建议治疗剂量按孕前体重计算(如依诺肝素 1 mg/kg、每日 2 次,达肝素钠 100 U/kg、每日 2 次),目标为 4~6 h 抗 Xa 峰值为 0.6~1.2 kU/L^[233-235]。通常情况下,UFH 用于高危 PE 的急性期治疗。溶栓只能用于严重低血压或休克的患者。当给予血栓溶栓后,不建议 UFH 负荷剂量,并以 $18 \text{ U} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ 开始输注。在患者稳定后,UFH 可以切换到 LMWH。如果对 LMWH 过敏或有不良反应,可考虑使用磺达肝羧酸钠(7.5 mg、每日 1 次,体重正常的孕妇)。腔静脉滤器的适应证与非怀孕患者相同,然而经验有限,可能会增加手术相关的风险^[66, 90]。对于近期发生 PE 的患者,如果没有发生明显出血,应在阴道分娩后 6 h 和剖腹产后 12 h 重新开始产前肝素治疗,随后与华法林重叠至少 5 d。华法林可在分娩后第 2 天开始,抗凝疗程维持至产后 6 周并满足至少 3 个月。INR

应该在 2~3,需要定期监测,最好是每 1~2 周监测 1 次。华法林不会以活性形式进入母乳,对哺乳期的母亲是安全的。了解怀孕期间心血管疾病的相关风险及其对患有严重既往疾病孕妇的管理、孕前宣教至关重要^[20, 236-237]。

4.5 避孕及孕期特殊情况下终止妊娠状态的管理: 建议最好由接受过专业培训的心脏病专家或产科医生提供,并应从初潮时开始提供,必须避免意外怀孕。关键问题是并发症的可能性,其中血栓形成和感染是最重要的。激素避孕益处包括控制月经、预防贫血、减少痛经^[238]。含有炔雌醇的避孕药具有最大的血栓风险,不建议具有血栓栓塞性疾病病史的高危妇女使用^[239-240]。可以单纯选择对凝血因子、血压和血脂水平影响小的孕激素避孕(如植入或储存注射)或完全没有影响的方式避孕(如含左炔诺孕酮的宫内节育器或口服去孕酮)^[241]。口服去孕酮抑制排卵可能是多囊卵巢综合征、子宫内膜异位症或功能失调性子宫出血患者的优势。其他方式如紧急避孕、宫内节育器等,如果在无保护性行为后 72 h 内服用单剂量 1.5 mg 左炔诺孕酮也是非常有效的方式(失败率为 1.1%)^[242],也没有证据表明血栓发生率增加^[243]。孕酮受体调节剂醋酸乌利司他(UA)已被证明比左炔诺孕酮更有效。UA 与血栓形成风险增加无关^[244-245]。

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