

# 早产儿体格及神经发育特点与预后

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**摘要:**早产儿的预后是全球范围内较为关注的热点问题。近年来,随着“二孩”政策的全面开放,高龄孕产妇及危重孕产妇数量逐渐上升,早产儿数量也随之增多。由于早产儿的体格及神经发育不成熟,易出现脑性瘫痪、智力低下、运动及认知障碍和远期神经、心理等相关后遗症。尽管医疗技术的进步改善了早产儿的存活率,但存活的早产儿更易发生学业障碍或行为障碍,甚至需要特殊教育,其远期预后备受关注。因此,研究早产儿体格及神经发育的特点,及时采取有效措施进行早期干预,对改善其预后尤为重要。本文主要综述早产儿体格及神经发育的过程、特点及预后,以期临床改善此类患儿的预后提供帮助。

**关键词:**早产儿;体格发育;神经发育;脑性瘫痪;认知障碍

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## Characteristics and Prognosis of Physical and Neurological Development of Premature Infants

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**Abstract:** The prognosis of premature infants is a hot issue of global concern. In recent years, with the full liberalization of the "two-child" policy, the number of pregnant women with advanced age and critically ill pregnant women has gradually increased, and the number of premature infants has also increased. Because of the immature physical and neurological development of premature infants, cerebral palsy, mental retardation, motor and cognitive impairment, and long-term neurological and psychological sequelae are prone to occur. Although advances in medical technology have improved the survival rate of preterm infants, surviving preterm infants are more prone to academic or behavioral disorders, and even require special education, and their long-term prognosis has attracted much attention. Therefore, studying the characteristics of physical and neurological development of premature infants and taking effective measures in time for early intervention are particularly important to improve their prognosis. This article mainly reviews the physical and neurodevelopmental process, characteristics and prognosis of premature infants, with a view to clinically improving the prognosis of such children.

**Key words:** Premature infants; Physical development; Neurodevelopment; Cerebral palsy; Cognitive impairment

2017年美国妇产科医师学会(ACOG)早产指南将早产定义为妊娠不满37周(259 d)的分娩儿。关于早产的孕周目前没有明确的下限,不同国家对其定义不同。在欧洲,早产的孕周下限可低至22周。据第9版《儿科学》,目前我国对于早产儿的分类主要有两种:①根据胎龄分为:极早早产儿(胎龄<28周),早期早产儿(28周≤胎龄<32周),中期早产儿(32周≤胎龄<34周)及晚期早产儿(34周≤胎龄<37周);②根据出生体重分为:超低出生体重儿(体重<1000 g),极低出生体重儿(体重<1500 g)和低出生体重儿(体重<2500 g)。2012年5月2日WHO首次就早产儿问题召开专题会议,发布《全球早产儿报告》,指出早产已经成为全球关注的公共卫生问题,并将每年的11月17日设立为“世界早产儿日”。基于此,本研究主要对早产儿体格及神经发育特点与

预后进行综述,以期临床治疗早产儿提供参考。

### 1 早产儿流行病学史

全球范围内的早产儿数据显示,早产的发生率与经济发展和医疗水平密切相关,早产儿发生率大于15%的国家共有12个,均为发展中国家,其中10个为非洲国家,2个为亚洲国家,而早产儿发生率低的国家多为发达国家,出生的早产儿中约有1100万集中在非洲和亚洲。早产儿出生数量前3位的国家分别是印度、中国及尼日利亚<sup>[1]</sup>。我国是早产儿大国,新生儿协作网报道,我国每年约1500万新生儿,其中150万为早产儿,且早产儿数量以每年增加20万的速度递增,华中地区、华东地区及华南地区早产儿发生率最高,分别为11.5%、10.99%、10.83%,华北地区早产儿发生率最低,为4.76%。

随着NICU技术和围产医学的迅猛发展,极早早产儿和极低出生体重儿抢救成功率显著提高,但由于其出生后各器官发育不成熟,缺乏孕后期的营养储备(如脂肪、糖及铁等),导致机体调节功能差<sup>[2]</sup>,使早产儿住院期间易发生呼吸窘迫综合征(NRDS)、支气管肺发育不良(BPD)、颅内出血、脑室周围白质损伤、新生儿坏死性结肠小肠炎(NEC)及早产儿视网膜病(ROP)等呼吸系统、神经系统及消化系统等多种并发症,严重影响了早产儿的生存质量。此外,

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早产还会导致如脑性瘫痪、感觉障碍、学习障碍、精神发育迟滞等远期影响<sup>[3]</sup>。

研究表明<sup>[4-6]</sup>,极早早产儿约占早产儿总数5%,尽管所占比例较低,但因其住院期间死亡率最高,且出院后的平均患病、残疾率为36%,因此极早早产儿的预后也备受关注。早期早产儿及中期早产儿数量约占早产儿总数的15%,住院期间仅需相应的支持治疗就可存活,但存活的早期及中期早产儿出院后由于智力、运动和行为功能受损,该群体多在初中毕业后结束学业<sup>[7-9]</sup>。早产儿比例最大的是晚期早产儿,约占早产儿总数的80%左右,其预后远好于早期早产儿及中期早产儿,晚期早产儿因住院时间短,仅需适当的护理及较少的医疗支持就能生存,故其长期并发症的风险常常被低估。晚期早产儿也存在较多神经发育不良后果,包括认知缺陷、学习困难和行为问题。研究表明,晚期早产儿的不良发育风险与足月儿相比有所增加,较足月儿相比更难完成学业,其智力低下的风险略高于足月儿童<sup>[10-12]</sup>。

## 2 早产儿体格发育特点

胎儿期是人生体格发育最快的阶段,也是体格发育最重要的阶段。在胎龄22~40周时胎儿经胎盘接受丰富的营养成分,用于组织生长发育。足月儿分娩时体重较妊娠22周时增长近6倍,而早产儿就出生在这个快速生长发育的阶段<sup>[13]</sup>。早产儿出生后的体重增长速度主要与热卡摄入有关。一方面,由于早产儿缺乏孕晚期的营养储备,且各器官发育不成熟,容易出现消化、呼吸、神经等系统疾病及多种并发症,使其热卡消耗增加;另一方面,由于其消化系统不成熟,胃肠道动力欠缺、吸吮-吞咽不协调,易发生喂养不耐受,故早产儿出生后几周内其体重很难达到正常足月儿的宫内增长速度。尽管有部分早产儿可在出院后甚至住院期间追赶性生长,但是仍有许多早产儿出院后生长速率小于相应胎龄生长速度的期望值<sup>[14]</sup>。这种现象被称作宫外发育迟缓(extrauterine growth retardation, EUGR),即出院时的体重、身长或头围低于相应胎龄的第10百分位。

近年来对EUGR的研究也是儿科领域的一个热点问题。国外研究显示,极早早产儿在纠正胎龄32周时,其生长发育指标仍低于同胎龄的第10百分位水平。国内研究证实,出生体重和胎龄是早产儿发生EUGR的危险因素,且EUGR发生率与胎龄及出生体重呈负相关。与宫内生长发育相比,EUGR对早产儿的影响更为重要<sup>[15-17]</sup>。部分早产儿因缺失宫内生长最快的阶段,出生后体内的脂肪和糖等营养储存不足,仅有的能量也由单纯满足生长需要变成应对各种生存需求,加之脱离母体后体内蛋白质供给中断,导致内源性蛋白质丢失,使早产儿住院期

间的营养摄入远低于同胎龄儿宫内的水平,甚至整个住院期间都处于营养缺乏状态。因此早产儿生后不进行积极营养支持,会加剧蛋白质及能量的进一步丢失,影响其预后。长期的蛋白及能量缺乏会影响早产儿头围、身长的发育<sup>[18]</sup>,从妊娠开始到生后5~6岁是大脑发育的关键期,而头围的增长情况反映了大脑的发育情况。因此头围的增长对早产儿的智力、认知、运动等各方面都有较大影响<sup>[19,20]</sup>。

相关研究表明,EUGR的早产儿中有15%存在严重的神经发育功能障碍。即使在没有重大疾病的情况下,仍有30%~50%的早产儿在运动、认知和行为方面存在轻度障碍<sup>[21-25]</sup>。在对学龄前儿童的调查中发现,EUGR儿童大部分可以在正常学校就读,但在学习、日常生活和表演等方面常遇到困难,且学习成绩常较差<sup>[26,27]</sup>。同时,EUGR儿童由于出生后一段时间内存在营养的缺乏,常常导致脂肪代谢紊乱,增加了青春期患肥胖症、心血管疾病及代谢综合征的风险。个别ELBW合并EUGR的儿童,其生长发育迟缓可持续至儿童时期<sup>[28,29]</sup>。因此,对EUGR儿童应进行长期随访,动态监测生长发育情况,拟定个体化的干预方案,减少EUGR对早产儿神经系统功能、心理等方面的影响,提高其生存质量。

## 3 早产儿神经发育特点

早产及低体重是影响小儿神经发育的重要因素<sup>[30]</sup>。人脑的发育始于胚胎发育的第3周,在胚胎的第25天神经元出现增殖,第33天起神经元分化为干细胞和胶质细胞,并在妊娠3~4个月达到高峰。随着神经元的产生,它们迁移到不同的大脑区域,进行大幅度调整,与其他神经元建立联系,突触快速形成、修建、重塑,形成复杂的神经网络。第8周时,神经管逐渐形成,并分化出间脑、中脑等结构,约至20周时出现端脑的外形。直到神经元迁移的最后阶段,这些细胞产生表达氨基丁酸(GABA)的神经元,它们是大脑的抑制性神经元<sup>[31]</sup>。在足月妊娠后期,GABA达到峰值,而GABA也被认为在早产儿脑损伤的发展影响中起作用。从胚胎形成至妊娠结束这段时间内,皮层和皮层下结构都得到快速发展和完善<sup>[32]</sup>。在出生早期,整个发育中的大脑的连通性水平远远超过了成年人<sup>[33]</sup>。出生后大脑也一直处于发育阶段,直至学龄前期,大脑的体积较出生后增加4倍,到6岁时基本可达到成人大脑体积的90%。

早产儿大脑结构的改变与多种因素有关,其中包括脑血管发育不成熟、脑室周围血管出血、大脑皮层或脑白质损伤等。早产儿因较早离开母体,出生时神经系统发育不成熟,脑细胞数量较少、血管发育欠佳、沟回少、白质髓鞘化未完成<sup>[34]</sup>。因此早产儿的脑室周边区域比足月儿更脆弱,极易破裂出血。而脑室

周围及脑室内出血可造成周围的静脉血液回流障碍,导致静脉栓塞<sup>[35]</sup>。研究表明,早产儿的小脑出血性损伤与远期神经发育障碍相关。围产期脑损伤最常见的类型是脑室周围白质损伤<sup>[36,37]</sup>。由于早产儿脑白质和皮层灰质体积小、脑白质区域少突胶质前体细胞尤其脆弱、对损伤非常敏感,因此极易发生脑室周围白质损伤。白质的损伤通常与认知能力受损、神经感觉异常有关。而大脑皮层损害除了引起运动障碍外,还常常与癫痫、认知和心理障碍有关。

此外,新生儿重症监护室处于高噪声水平、加之频繁的强光照射以及母婴分离等交杂一起形成一种高压环境。早产儿长期存在于压力环境中加上急性疼痛刺激,其可能处于一种应激状态,这种状态并不利于神经发育,并且可能导致早期神经系统损伤以及远期神经发育的不良预后<sup>[38,39]</sup>。大脑的常态发展、运行以及环境输入对于正常的大脑发育都是必不可少的,而两者的破坏都可以从根本上改变神经的结局。

从胚胎形成至生后5~6年,是大脑发育最关键、最迅速的阶段,也是其可塑性的敏感阶段。可塑性是指大脑在外界刺激下可发生结构和功能重塑的巨大潜能。环境的变化可改变神经元的大小、突触的数目、脑的整体结构。对早产儿进行早期以及长期随访,提高其生存质量,正是基于大脑这种可塑性的生物学基础<sup>[40,41]</sup>。尽管NICU技术的不断进步,使早产儿的生存率逐步提高<sup>[42]</sup>,但存活的早产儿神经系统损害依然常见。因此利用早产儿大脑可塑性的生物学基础,对其进行早期干预,在脑发育的关键时期给予良性刺激,可促进突触发育,改善脑功能,加快大脑发育速度。

研究显示,美国的早产儿因大脑发育不成熟导致的脑性瘫痪所产生的医疗费用每年可增长10~25倍<sup>[43]</sup>。因此对早产儿进行长期动态随访,有目的、有计划的采取相应的早期干预措施,促进神经细胞生长,改善神经系统及大脑发育的结局,可预防早产儿潜在问题,改善早产儿的预后,提高其生存质量,从而减轻家庭和社会的经济负担。

#### 4 总结

早产儿已成为全球范围内的公共卫生问题,尽管存活的早产儿住院期间及出院后的不良预后、风险因素已被证实,但相关报道显示极早早产儿出院后的平均患病、残疾率仍居高不下,并且目前对极早早产儿的早期干预是否有效还存在争议。然而不可否认的是,早期干预对改善中晚期早产儿的预后有积极作用。作为妇产科医师,应该详细了解早产儿的危险因素及现状,加强围产期保健,减少早产的发生率,同时提高复苏水平、熟练掌握救治早产儿的核心技术;作为儿科医师,需加强早产儿入院

前及出院后的综合管理,强化家长对于早产儿出院后规律随访的意识,保证家长对出院后长期随访的医从性,做到规律、动态随访,及时尽早干预,提高早产儿的预后。

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