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(收稿日期: 2015-05-08)

·综　　述·

空腹血糖水平与冠心病的关系*

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关键词: 冠心病;　血糖;　危险因素
DOI: 10.3969/j.issn.1673-4130.2015.22.029　　**文献标识码**: A　　**文章编号**: 1673-4130(2015)22-3289-03

血糖代谢异常在冠心病患者中相当普遍, 表现为空腹血糖、餐后血糖和糖化血红蛋白的异常[1]。针对既往糖尿病或新

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确诊糖尿病患者为期一年的一项随访调查表明，与普通人群比较，糖尿病患者有更高的心血管事件发生率或死亡风险[2]。同样，合并有糖尿病的冠心病患者较单纯的冠心病患者病变更为严重，动脉粥样硬化的相关指标改变更为明显。糖尿病与冠心病有共同的致病基础[3]。笔者在前期研究中发现，即使是血糖处于正常参考范围，同期入院心内科的患者，确诊为冠心病的患者其入院后的第一次空腹血糖水平高于除外冠心病的其他患者[4]，这引起了笔者对血糖水平与冠心病关系的兴趣。本文综合分析了国外近二十余年针对血糖与冠心病相关研究，根据患者空腹血糖水平分组，综述不同血糖水平与冠心病病变严重程度及结局的相关性。

1 低血糖对冠心病的影响

低血糖定义为空腹血糖水平小于 3.9 mmol/L，严重的低血糖定义为空腹血糖水平在 2.2～2.8 mmol/L 范围内。有研究表明，糖尿病患者降糖过度造成的低血糖可增强氧化应激、促进动脉粥样硬化、引起炎症反应和内皮细胞功能紊乱等，从而引发糖尿病患者的血管并发症[5]，其中，炎症反应和内皮功能紊乱被认为是糖尿病血管并发症的主要原因[6]。此外，低血糖还与不合并心血管疾病的糖尿病患者的突然死亡有关系[7]。低血糖常为糖尿病患者或者入院应急高血糖强化治疗后的不良反应。糖尿病控制与并发症研究/糖尿病干预及并发症流行病学研究(DCCT/EDIC)经过 6 年的观察得出结论，认为针对 1 型糖尿病患者的强化治疗可降低其肾脏疾病、心血管疾病和神经病变等并发症的风险，所以主张积极的降糖治疗[8-9]。英国的一项更为广泛的前瞻性研究却表明，针对 2 型糖尿病患者的强化治疗不仅没带来心血管疾病并发症的降低，反而增加了低血糖的发生率，从而引发更为严重的后果[10-11]。目前，关于尿病患者的强化治疗是否增加心血管疾病的风险，还存有争议，有待于进一步研究，但是鉴于低血糖造成的严重后果，对于糖尿病治疗药物的选择，要慎重考虑其带来的低血糖风险[12]。

2 正常血糖与冠心病的相关性

空腹血糖处于正常参考范围人群的血糖水平与冠心病发病及结局也有报道。有一项针对伊朗人血糖正常、糖耐量正常的调查表明，胰岛素抵抗[空腹血清胰岛素水平(μU/mL)×空腹血糖水平(mmol/L)/22.5]的水平与高血压、高三酰甘油和低高密度脂蛋白这些心血管疾病的传统危险因素相关[13]。韩国的一项针对非冠心病人群的调查表明，稍高一些的糖化血红蛋白水平与亚临床的心脏冠状动脉粥样硬化独立相关[14]。以色列一项平均追踪 4.3 年的研究表明，血糖在正常范围内的人群，较高的血糖水平与增高的冠心病发病风险独立相关[15]。Petersen 等[16]在美国杜克大学医学中心的一项持续 5 年针对新发冠心病人群的联合调查表明，合并有糖尿病的患者病死率会升高，而合并代谢综合征的患者病死率与无代谢综合征及糖尿病患者的病死率无明显差异。

3 糖尿病前期的空腹血糖水平与冠心病的相关性

糖尿病前期定义为空腹血糖水平在 5.6～6.9 mmol/L 范围内波动。虽然不是所有的糖尿病前期患者都会进展为糖尿病患者，但是这部分人群进展为糖尿病的比例还是高于普通人群，糖尿病前期每年以大约 10% 的比例进展为糖尿病[17]。一般而言，不容易发现冠心病合并糖尿病前期或者无症状糖尿病的现象[18]。同时，不仅糖尿病患者的冠状动脉及分支的管腔直径要小于对照人群，而且临床实践中发现，即使在糖尿病前期也有这样的现象[19]。相反，Xing 等[20]一项针对糖尿病前期人群的队列研究，并没发现入组时的空腹血糖水平和/或糖化血红蛋白水平与亚临床的动脉粥样硬化及肾功能受损独立相关，该研究认为除去其他心血管危险因素的干扰，糖尿病前期本身不会增加普通人群的动脉粥样硬化及肾脏病的风险。近期，土耳其的一项联合研究发现，糖尿病前期不依赖于性别与心脏血管的弥漫性狭窄有关，特别是冠状动脉远端和左前降支远端的狭窄[21]。事实上，这种心脏小血管的弥漫性狭窄会给临床带来更多的麻烦，对于常规的介入治疗及搭桥手术治疗有更高的技术要求，治疗后也相对容易造成再狭窄[21]。

4 糖尿病期空腹血糖水平与冠心病的关系

无论 1 型还是 2 型糖尿病，冠心病是糖尿病患者主要死亡原因[1,22]。2 型糖尿病患者因心血管意外死亡的风险是普通人群的 2 倍，与既往有心肌梗死史，不伴有糖尿病患者的心血管意外死亡风险相当[23-24]。与不合并糖尿病的冠心病患者相比，合并糖尿病的冠心病患者接受经皮冠状动脉腔内成形术(PTCA)后，无论是裸支架还是药物支架都易于造成不良结局，包括再狭窄及其他心血管事件[25-26]。Fu 等[27]联合欧洲的七个国家共同进行的针对合并有冠心病的糖尿病患者治疗情况的调查发现，合并有冠心病的糖尿病患者并没有向预先设想的那样，相对于没有合并冠心病的糖尿病患者血糖控制更好。糖尿病患者血糖控制达标有利于减少并发症，合并有冠心病的糖尿病患者未来有更高的心血管意外死亡风险，这部分人群应该有更为严格的血糖控制。

总之，糖、脂肪、蛋白质人体这三大供能物质的代谢彼此联系，相互转变、相互依存，构成统一的整体，三大物质以乙酰辅酶 A 为纽带有共同的代谢池。血脂作为冠心病的危险因素已达成共识，而血糖作为人体供能的核心，其对于心脏的影响目前所知道的还不够多。

目前，针对血糖与冠心病二者关系的研究不多，也未有统一的结论。未见有利用血清葡萄糖水平诊断冠心病的报道，血清葡萄糖水平对冠心病的诊断价值不清楚，但是鉴于二者的密切关系，笔者考虑可以尝试危险分层的办法。在原有的心血管疾病的危险因素基础之上，加上血清葡萄糖水平这一参数，是否能够对患者未来发生冠心病的风险做进一步的预测，尚不清楚。随着大数据时代的到来，会有更多的临床数据支持，利用血清葡萄糖水平结合传统冠心病危险因素做出对冠心病更为细化的危险分层，或许是未来诊治冠心病的另外一种途径。

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(收稿日期: 2015-06-22)

·综　　述·

血药浓度监测技术进展的研究

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关键词: 治疗药物监测;　荧光偏振免疫分析;　高效液相色谱法
DOI: 10.3969/j.issn.1673-4130.2015.22.030　　**文献标识码**: A　　**文章编号**: 1673-4130(2015)22-3291-04

治疗药物监测(TDM)在临床指导合理用药、制定个性化给药方案中应用广泛。监测血液中药物或其代谢物浓度是临

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