·卷首语·

丰富中国 2 型糖尿病防治措施的临床证据链，建立基于中国人群证据的糖尿病防治指南——纪念第 1 版《中国 2 型糖尿病防治指南》发布 10 周年

纪立农

Develop Chinese diabetes guidelines from clinical evidence in China——Marking the tenth anniversary of the first edition of Chinese diabetes guidelines for type 2 diabetes *JI Li-nong. Department of Endocrinology, Peking University People's Hospital, Beijing 100044, China*

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2013 版《中国 2 型糖尿病防治指南(征求意见版)》(下称“指南”)已公布。新版指南公布距离我国第 1 版《2 型糖尿病防治指南》发布整整 10 年。

2003 年，中华医学会糖尿病学分会在中国糖尿病杂志名誉主编，时任中华医学会糖尿病学分会主任委员钱荣立教授的领导下制定了第 1 版《中国 2 型糖尿病防治指南》。该指南的出台结束了像中国这样的“糖尿病大国”依靠国际上的指南来指导中国糖尿病防治的历史，并为中国的糖尿病防治提供了临床证据。限于当时中国糖尿病临床研究基础仍较薄弱，2003 版指南所依据的临床证据主要来自于非中国人群。指南从体例上更接近教科书，并借鉴了国际糖尿病联盟西太平洋地区糖尿病指南“2 型糖尿病实用目标和治疗”和国际上其他糖尿病指南中的部分内容。2007、2010 及 2013 年对指南进行修订时更注重系统的收集在中国人群中产生的临床证据并使指南的体例更符合临床指南要求，即主要以基于临床证据的建议作为指南主体并辅以对证据的概括性总结。

随着我国糖尿病临床研究的广泛开展，在中国人群中产生的临床证据不仅限于描述中国糖尿病和并发症流行病学现况、疾病的控制现况和经济负担的临床研究的证据[1-12]。越来越多的证据[13-23]来自于基于中国普通人群的糖尿病和相关疾病的预测；多中心、前瞻性、随机分组对照的生活方式干预研究[24-25]和临床药物研究[26-53]；基于科学假设的前瞻性、多中心、平行对照药物临床研究[54]以及对在中国 2 型糖尿病人群和包括中国 2 型糖尿病患者在内的亚洲人群中所开展的随机分组临床试验的 Meta 分析[55-57]。研究目标也从单纯评价药物降糖疗效和安全性扩展到评价药物对心血管疾病结局的影响[29]。但与在国外人群中开展的临床研究相比，降糖药物治疗在中国的临床证据仍十分匮乏(如影响血糖的因素众多，当前在国际上公认的评价药物降糖疗效的最客观方法是通过安慰剂对照的随机分组对照研究来客观评价降糖药物疗效。但迄今为止尚缺乏高质量的，在我国广泛使用的双胍类药物、磺脲类药物、α-糖苷酶抑制剂、格列奈类药物和吡格列酮的针对安慰剂对照的临床证据)。从严格的循证医学证据角度来讲，我们尚不知上述药物在中国 2 型糖尿病患者中的降糖效果是否强于安慰剂。因此，分别以在中国人群中降糖幅度不明的磺脲类药物和α-糖苷酶抑制剂作为参照药物在中国 2 型糖尿病患者中所评价的胰升血糖素样肽-1(GLP-1)受体激动剂利拉鲁肽[53]和二肽基肽酶-4(DPP-4)抑制剂维格列汀单药治疗[37]所得到的、与上述参照药物非劣效的临床试验结果仍使利拉鲁肽和维格列汀单药治疗的降糖疗效处于“未知状态”。

可喜的是，新近在我国上市的一些新型降糖药物，如西格列汀(单药和联合治疗)[34-35]、维格列汀(联合治疗)[36]沙格列汀(单药和联合治疗)[38-39]、安

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格列汀(联合治疗)[40]、艾塞那肽(联合治疗)[52]已在中国 2 型糖尿病患者中完成了与安慰剂对照的多中心、前瞻性随机分组的临床研究,获得了明确疗效的临床证据,为临床医生选择用药提供了重要的参考依据。

传统医学手段在当前中国糖尿病的治疗中占有非常大的比重。尽管我国是一个中医、中药大国,但迄今为止,仅有数个研究采用多中心、前瞻性、随机分组、双盲、安慰剂对照的方法评价了中药或中药中的主要成分在治疗和预防糖尿病的作用[27,41-43]。

胰岛素类似物已在中国糖尿病患者中得到比较广泛的使用。但其价格昂贵,所以在中国人群中是否比人胰岛素提供更多的临床益处则需要临床证据的支持。目前,仅有甘精胰岛素(Glargin)与传统的基础胰岛素——中效人胰岛素(NPH)[45]及速效胰岛素——赖浦胰岛素(Lispro)预混制剂[46-47]与人胰岛素预混制剂之间的多中心、随机分组、前瞻性对照研究的临床证据,尚缺乏在中国糖尿病患者中速效胰岛素赖浦胰岛素(Lispro)与常规人胰岛素,胰岛素类似物地特胰岛素(Detemir)与中效人胰岛素(NPH)及速效胰岛素门冬胰岛素(Aspart)及其预混制剂与人常规胰岛素及其预混制剂之间的多中心、随机分组、前瞻性对照研究的临床证据。少数研究采用了多中心、随机分组、前瞻性对照研究的方法对照了不同的胰岛素类似物治疗方案间的疗效与安全性[48-49]。

当前,我国仍缺乏中国人群中与糖尿病最直接相关的糖尿病急性并发症、糖尿病微血管并发症的疾病自然病程和治疗策略的临床证据。

2 型糖尿病是一种或多种心血管疾病危险聚集而以心血管疾病为主要结局的疾病。目前,根据国际上的循证医学证据,用于降低胆固醇的他汀药物、抗血小板聚集的药物及降压药物已与降糖药物一同成为糖尿病的标准治疗措施。迄今为止,尚没有直接来自我国糖尿病人群中上述药物长期安全性和有效性的临床证据。最近,美国 AHA 公布了根据美国人群的循证医学证据所制定的美国成人胆固醇控制策略[58]后曾一度引起国内学界的一片喧嚣,但缺乏中国人群的证据使得这场喧嚣变成了苍白无力且无济于中国心血管病防治的夸夸其谈。

我们也非常高兴的发现,在最近几版的指南中,与糖尿病相关的重要临床问题,如儿童和青少年糖尿病,妊娠期糖尿病或糖尿病合并妊娠、抑郁、手术治疗糖尿病,糖尿病外周血管病变,低血糖,糖尿病教育,血糖监测,围手术期管理、感染,阻塞性睡眠呼吸暂停及口腔疾病得到高度的重视。但与上述问题相关的临床证据来源仅限于临床流行病学和观察性研究。绝大多数与诊治策略相关的临床证据来自非中国人群的研究结果,仅少数来自国内的初步研究[50,59-62]。

目前,中国是全球的糖尿病大国。根据国际糖尿病联盟估计,中国 2013 年糖尿病患病人数为 9840 万,居世界各国糖尿病患病人数的首位。到 2035 年,中国糖尿病患病人数将达 1.43 亿,仍居全球首位。虽然目前有限的临床证据并不支持疾病的防治策略和防治手段,但因遗传背景、生活习惯、文化差异和医疗环境等诸多因素所带来的疾病防治手段在不同人种间和不同环境居住中的人群间效果差异存在的可能性仍存在。对占世界近四分之一的中国糖尿病人群防治不能一直依靠来自其他人群的临床证据。

古人云,“十年磨一剑”,欲使指南成为在我国与糖尿病抗争中“削铁如泥”的利剑,我们不但要光其表面,更重要的是炼其材质。

今后,我国不但要加紧补课,将中国 2 型糖尿病防治的证据链中相对于其他人群缺失的环节逐渐补充进来,且要根据中国糖尿病防治中未被满足的需求有的放矢的建立新的临床证据。只有建立在充足的来自中国人群临床证据的糖尿病防治指南,才能更好地指导中国糖尿病防治的临床实践并逐渐使中国从临床证据的进口国成为临床证据的出口国,担负起参与和领导全球糖尿病防治的“大国”重任。

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