

2型糖尿病与房颤的相关性研究进展

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收稿日期: 2025年9月21日; 录用日期: 2025年10月14日; 发布日期: 2025年10月21日

摘要

2型糖尿病(T2DM)是全球心血管并发症的主要危险因素。心房颤动(AF)是最常见的室上性心律失常。两者的发病率都呈逐年上升。大型研究和荟萃分析表明AF和T2DM之间存在明显联系, 从而确定了T2DM患者发生AF的风险。基于这两种疾病与心血管疾病发病率和死亡率的高风险之间的联系。在本篇综述中, 我们结合这两种实体的病理生理机制, 以及现有可用于AF糖尿病患者的治疗方案, 为其提供最新依据。

关键词

2型糖尿病, 房颤, 相关性分析

Research Progress on the Relationship between Type 2 Diabetes Mellitus and Atrial Fibrillation

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Received: September 21, 2025; accepted: October 14, 2025; published: October 21, 2025

Abstract

Type 2 diabetes mellitus (T2DM) is a major risk factor for cardiovascular complications worldwide. Atrial fibrillation (AF) is the most common supraventricular arrhythmia. The incidence rate of both has increased year by year. Large scale studies and meta-analyses have shown a clear association

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between AF and T2DM, thus determining the risk of AF in T2DM patients. Based on the association between these two diseases and the high risk of cardiovascular disease incidence rate and mortality. In this review, we combine the pathophysiological mechanisms of these two entities, as well as the existing treatment schemes for AF diabetes patients, to provide the latest basis for them.

Keywords

Type 2 Diabetes Mellitus, Atrial Fibrillation, Correlation Analysis

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1. 引言

心房颤动(房颤)是最常见的心律失常性疾病之一,与心源性卒中、心力衰竭(心衰)和心血管死亡密切相关。目前我国糖尿病患者人数已超过 1.4 亿,居世界首位大型研究和荟萃分析表明 AF 和 T2DM 之间存在明显联系,从而确定了 T2DM 患者发生 AF 的风险,两者的共病管理是临床实践中的一个重要挑战和热点。本研究运用数据库(PubMed、Web of Science 核心合集、中国知网(CNKI)和万方数据知识服务平台),采用主题词与自由词相结合的方式检索。重点检索 2000 年 1 月至 2024 年 6 月期间发表的文献,以确保涵盖该领域的重要基础研究和最新进展。通过以上策略,初步检索获得相关文献,经阅读标题、摘要和全文后,最终筛选出与本综述主题最相关的核心文献进行归纳、分析和述评。

2. T2DM 与 AF 的相关性

糖尿病与许多代谢缺陷相关,包括胰岛素抵抗,糖耐量受损、促炎介质、异常止血、纤维蛋白溶解、血管生成和细胞外基质等。所有这些代谢变化都会导致内皮功能障碍、肾素-血管紧张素-醛固酮系统(RAAS)异常激活和动脉粥样硬化形成,可能是 AF 发生的原因。

2010 年的一项研究表明,糖尿病患者发生房颤的风险增加 40%,2011 年,在非糖尿病人群中,T2DM 患者发生房颤的风险为 34% [1],在 2017 年的荟萃分析中,在前瞻性队列研究中,较高的血清糖化血红蛋白水平(HbA1c)与 AF 发病相关[2]。同样,在 NOMED-AF 前瞻性横断面观察研究中,研究人员得出结论,AF 影响四分之一的 T2DM 患者,这突出表明糖尿病人群需要 AF 筛查[3]。

2022 年,对 21 项研究的荟萃分析得出结论,患有 T2DM 的 AF 患者具有较高的心血管和全因死亡率风险[4]。同样,在早期的 ADVANCE 研究中,与无房颤的糖尿病患者相比,患有房颤的 T2DM 患者发生重大心脑血管事件以及心血管和全因死亡的风险增加[5]。

3. 病理生理学

3.1. 结构改造

从动物研究中获得的大多数证据表明心房扩张和间质纤维化是 AF 的主要触发因素。而房颤引起最显著的结构改变就是心房扩张和纤维化。由于心肌纤维化与 T2DM 独立相关,糖尿病患者有显著的 AF 发生底物,更具体地说,T2DM 与心肌纤维化相关的细胞和分子基础机制包括长期高血糖引起的炎症和氧化应激[6]。在糖尿病患者中,活性氧(ROS)的产生增加,而降低 ROS 的酶的表达减少,这表明氧化应激负荷较高[7]。高氧化应激负荷可导致并加重先前存在的炎症和炎症标记物,如 C 反应蛋白和肿瘤坏死

因子- α , 与左心房扩张和房颤发病率增加相关[8]。T2DM 上调促纤维化生长因子的表达, 如转化生长因子(TGF)- β , 它激活促纤维化途径[9]。纤维化会减缓心房传导, 并为重返心房创造基质[10]。

3.2. 电气改造

心房电重构的主要特征涉及心房有效不应期缩短和分散, 以及频率适应受损和随后的心房间传导延迟。糖代谢异常的患者可能会出现传导异常, 例如激活时间延长[11]。动物研究的实验数据表明, T2DM 与异常电流密度、心房传导和不应期有关, 所有这些都增加了 AF 的易感性[12]。除了电重构和传导重构外, T2DM 还可以影响心房兴奋-收缩耦合, 导致机电延迟(EMD)和心律失常发生, 因为 EMD 是新发和复发房颤的独立预测因子[13]。糖尿病患者消融术后房颤复发率较高, 可能是电重构引起的心律失常前基质所致。

3.3. 自主重构

研究表明, 糖尿病患者的心房组织有更大的能力摄取胆碱和释放乙酰胆碱。T2DM 引起的心脏自主神经病变有助于副交感神经的缩小和交感刺激的上调, 导致自主神经失衡, 从而刺激心律失常, 如房颤[14]。一项针对 1992 名 T2DM 患者的横断面对照研究表明, 自主神经功能障碍与源于自主神经功能障碍的 T2DM 患者的无症状房颤之间存在密切关系[15]。

3.4. 血糖水平

T2DM 患者可能会出现低血糖, 这会传播交感神经激活和过度兴奋, 导致房颤风险增加[16]。而强化血糖控制并不能降低房颤的风险, 这可能是由于严重低血糖引起的交感神经过度兴奋所致[17]。另一方面, 慢性高血糖也为心房重构和房颤的发生创造了基础。高血糖也与血管紧张素 II 信号转导活性氧生成增强有关[18]。此外, 高糖水平可通过生成 AGEs 增强纤维化, AGEs 可通过激活其表面受体调节心脏成纤维细胞。然而, 研究发现, 实际上是血糖波动, 而不是慢性高血糖, 可能会增加房颤的风险, 因为它们会导致氧化应激和心房纤维化[19]。同样的研究也强调了随着血糖水平的升高, 房颤风险升高。在最近对糖尿病和房颤患者的亚分析中, 进一步报告了血糖控制不佳会增加房颤风险[20]。

3.5. 肥胖

大量研究表明糖尿病是房颤的独立危险因素, 与房颤共存的沉淀环境有关[21]。肥胖趋势是最典型、最臭名昭著的风险因素之一, 它密切反映了 T2DM 的流行趋势。在美国, 61%至 85%的 T2DM 患者超重或肥胖[22]。此外, 肥胖也是 AF 的既定风险因素。与非肥胖者相比, 肥胖比普通人群患 AF 的风险增加了 49%, 并且风险与体重指数(BMI)平行上升[23]。在弗雷明翰心脏研究中, BMI 每增加一个单位, AF 风险就会增加 4%~5% [24]。此外, 一项基于人群的研究表明, 每 1 和 5 kg/m² BMI 降低与新发 AF 风险降低 7%和 12%相关[25]。

4. 治疗

4.1. 抗糖尿病药物

关于糖尿病患者的治疗, 药物应旨在降低血糖水平并防止血糖波动。目前正在使用各种口服药物治疗 2 型糖尿病, 其中一些与房颤风险较低有关, 二甲双胍是最常用的口服药物。已被证明可以减弱炎症反应和氧化应激, 而不依赖于抗高血糖作用, 这在理论上可以降低 AF 的风险。二甲双胍下调炎症重要调节因子核因子 κ B 亚基 1(NF- κ B), 并减少促炎细胞因子的产生[26]。在一项针对 645,710 名患者的队列研究中, 与其他降糖药物相比, 二甲双胍单药治疗可使房颤风险降低 19%, 尤其是在确诊后的前两年[27]。

噻唑烷二酮类(TZD)通过作用于脂肪、肌肉和肝脏(在较小程度上)来增加胰岛素敏感性,以增加葡萄糖利用率并减少葡萄糖生成。通过增殖激活受体 γ 激动剂和过氧化氢酶的刺激,抗氧化作用可能更加明显[28]。大量文献表明,使用 TZD 可降低约 20%~30% 的 AF 发病风险,这是在丹麦一个全国性队列研究中发现的,该队列研究的受试者人数超过 100,000 人患有 T2DM [29]。

新型抗糖尿病药物,二肽基肽酶-4 (DPP-4)抑制剂是抑制外周血浆中 DPP-4 活性的降血糖剂,可防止外周循环中肠促胰岛素-胰高血糖素样肽-1 (GLP1)的失活。如前一项研究所示,与其他抗糖尿病药物相比,这些药物产生房颤的风险更低[30]。

钠-葡萄糖协同转运蛋白-2 (SGLT2)抑制剂通过在肾脏水平阻断过滤葡萄糖的再吸收来降低血糖水平。这些药物具有心脏保护作用[31]依赖于多种分子机制,包括恢复有益的自噬、抗氧化剂[32],消炎药[33]和抗纤维化反应。

4.2. 抗凝治疗

栓塞性卒中是房颤的一种毁灭性并发症,可能导致长期残疾,终身依赖或需要在疗养院住院,甚至死亡[34]。大多数房颤患者需要长期口服抗凝药物,以降低未来缺血性不良事件的风险[35],即降低栓塞性中风或全身栓塞的风险。与非糖尿病患者相比,T2DM 患者高血压、血管疾病、左心房扩大和左心室功能障碍的患病率更高[36]。直接(新型、非维生素 K 依赖性 VKA)口服抗凝剂(DOAC)具有一些优点,例如与 VKA 相比,更可预测的凝血抑制作用,更快的作用开始和抵消,更短的血浆半衰期,食物和药物相互作用的风险更低,无需对所获得的抗凝活性进行常规实验室监测。由于这些优点,DOAC 最近应该被优先用于房颤患者的长期口服抗凝。

基于 CHAD₂DS 公司 2-默认情况下,每个糖尿病患者都应考虑 VASc 风险评分、抗凝治疗。与华法林相比,直接口服抗凝剂(DOAC)可使中风事件减少 20%,颅内出血减少 43% [37]。此外,一项研究表明,DOAC 对 T2DM 患者和非糖尿病患者一样安全有效[38]。对于 T2DM 和 CHA 患者 2DS 公司 2-VASc 得分 ≥ 2 ,DOAC 可能优于华法林。2021 年一项针对糖尿病患者 OACs 的安全性(低血糖或出血)和有效性(中风或系统性栓塞)的系统综述得出结论,DOAC 比华法林具有更好的临床特征[39]。

4.3. 抗心律失常治疗

4.3.1. 药物治疗

药物复律:T2DM 作为共病,与心脏复律的疗效较差相关。到目前为止,各种研究表明,T2DM 导致 74.5 天随访时心脏复律即刻成功率较低,窦性心律维持成功率低,同时也被确定为 30 天内心脏复律失败的独立危险因素[40]。值得注意的是,尽管在房颤患者中有很高比例的患者可以看到自发复律,但在同时患有 T2DM 的患者中,其发生率明显较低[41]。

关于决奈达隆在 T2DM 中的应用,与安慰剂相比,它与较低的心血管住院率和死亡率以及更大的 AF 自由度有关[42]。同时,接受胺碘酮治疗的 T2DM AF 患者的特定亚组没有可用数据。然而,之前的一项研究表明胺碘酮对 T2DM 患者具有延迟抗心律失常作用,部分归因于糖尿病自主神经病变[43]。通常,由于伴随 QTc 延长、无症状冠状动脉疾病或肾功能衰竭,T2DM 患者可能更容易因抗心律失常药物治疗而产生不良反应[44]。尽管如此,Angelo 的一项研究等观察到,T2DM 患者不太可能中断规定的抗心律失常方案[45]。

4.3.2. 手术治疗

无论症状如何,早期心律管理对降低 AF 后果的负担至关重要[46]。经皮导管心房颤动消融是一种很有吸引力的心律调节技术。电生理学中最常用的消融治疗是射频导管消融。

有报道称, T2DM 患者导管消融的疗效低于非 T2DM 患者。这可能是因为诱导的瘢痕可能损害心房松弛, 促进 T2DM 患者的左心房僵硬表型[47]。Wang 等人据报道, 在校正基线差异后, 2 型糖尿病组在导管消融后心律失常复发率显著高于非糖尿病组(HR 2.24; 95% CI 1.42~3.55) [48]。此外, 我们发现 2 型糖尿病组和非糖尿病组手术消融术后 1 年和 3 年死亡率相似, 但 2 型糖尿病患者的 5 年死亡率较高。因此, 血糖控制程度可能是一个重要的混杂变量。大量研究表明, 较高的基础糖化血红蛋白水平与导管消融术后房颤复发率较高相关[49]。

5. 总结与展望

本文通过归纳和总结近些年来有关糖尿病与房颤相关性研究的最新进展, 其在结构、电生理和自主神经通路已被确定为潜在机制。因此, 我们还需进一步地探索其发病的根本原理。现有研究普遍存在样本量较小、种族性别等混杂因素控制不佳等局限性。关于治疗, 即可调控血糖又可抗心律失常和抗血栓的药物及治疗策略有待详细研究。考虑到糖尿病与房颤之间复杂的潜在致病机制, 临床实践中应当重视房颤患者的血糖管理, 开展高质量临床与基础研究, 为房颤疾病防治提供新的干预靶点与策略。

参考文献

- [1] Huxley, R.R., Fillion, K.B., Konety, S. and Alonso, A. (2011) Meta-Analysis of Cohort and Case-Control Studies of Type 2 Diabetes Mellitus and Risk of Atrial Fibrillation. *The American Journal of Cardiology*, **108**, 56-62. <https://doi.org/10.1016/j.amjcard.2011.03.004>
- [2] Qi, W., Zhang, N., Korantzopoulos, P., Letsas, K.P., Cheng, M., Di, F., *et al.* (2017) Serum Glycated Hemoglobin Level as a Predictor of Atrial Fibrillation: A Systematic Review with Meta-Analysis and Meta-Regression. *PLOS ONE*, **12**, e0170955. <https://doi.org/10.1371/journal.pone.0170955>
- [3] Gumprecht, J., Lip, G.Y.H., Sokal, A., Średniawa, B., Mitreğa, K., Stokwiszewski, J., *et al.* (2021) Relationship between Diabetes Mellitus and Atrial Fibrillation Prevalence in the Polish Population: A Report from the Non-Invasive Monitoring for Early Detection of Atrial Fibrillation (NOMED-AF) Prospective Cross-Sectional Observational Study. *Cardiovascular Diabetology*, **20**, Article No. 128. <https://doi.org/10.1186/s12933-021-01318-2>
- [4] Xu, J., Sun, Y., Gong, D. and Fan, Y. (2022) Impact of Preexisting Diabetes Mellitus on Cardiovascular and All-Cause Mortality in Patients with Atrial Fibrillation: A Meta-Analysis. *Frontiers in Endocrinology*, **13**, Article 921159. <https://doi.org/10.3389/fendo.2022.921159>
- [5] Du, X., Ninomiya, T., de Galan, B., Abadir, E., Chalmers, J., Pillai, A., *et al.* (2009) Risks of Cardiovascular Events and Effects of Routine Blood Pressure Lowering among Patients with Type 2 Diabetes and Atrial Fibrillation: Results of the ADVANCE Study. *European Heart Journal*, **30**, 1128-1135. <https://doi.org/10.1093/eurheartj/ehp055>
- [6] Russo, I. and Frangogiannis, N.G. (2016) Diabetes-Associated Cardiac Fibrosis: Cellular Effectors, Molecular Mechanisms and Therapeutic Opportunities. *Journal of Molecular and Cellular Cardiology*, **90**, 84-93. <https://doi.org/10.1016/j.yjmcc.2015.12.011>
- [7] Ziolo, M.T. and Mohler, P.J. (2015) Defining the Role of Oxidative Stress in Atrial Fibrillation and Diabetes. *Journal of Cardiovascular Electrophysiology*, **26**, 223-225. <https://doi.org/10.1111/jce.12560>
- [8] Guo, Y., Lip, G.Y.H. and Apostolakis, S. (2012) Inflammation in Atrial Fibrillation. *Journal of the American College of Cardiology*, **60**, 2263-2270. <https://doi.org/10.1016/j.jacc.2012.04.063>
- [9] Liu, C., Fu, H., Li, J., Yang, W., Cheng, L., Liu, T., *et al.* (2012) Hyperglycemia Aggravates Atrial Interstitial Fibrosis, Ionic Remodeling and Vulnerability to Atrial Fibrillation in Diabetic Rabbits. *The Anatolian Journal of Cardiology*, **12**, 543-550. <https://doi.org/10.5152/akd.2012.188>
- [10] Kato, T., Yamashita, T., Sekiguchi, A., Tsuneda, T., Sagara, K., Takamura, M., *et al.* (2008) Age-Related System Mediates Atrial Structural Remodeling in the Diabetic Rat. *Journal of Cardiovascular Electrophysiology*, **19**, 415-420. <https://doi.org/10.1111/j.1540-8167.2007.01037.x>
- [11] Tiwari, S., Schirmer, H., Jacobsen, B.K., Hopstock, L.A., Nyrnes, A., Heggelund, G., *et al.* (2015) Association between Diastolic Dysfunction and Future Atrial Fibrillation in the Tromsø Study from 1994 to 2010. *Heart*, **101**, 1302-1308. <https://doi.org/10.1136/heartjnl-2015-307438>
- [12] Chao, T., Suenari, K., Chang, S., Lin, Y., Lo, L., Hu, Y., *et al.* (2010) Atrial Substrate Properties and Outcome of Catheter Ablation in Patients with Paroxysmal Atrial Fibrillation Associated with Diabetes Mellitus or Impaired Fasting Glucose. *The American Journal of Cardiology*, **106**, 1615-1620. <https://doi.org/10.1016/j.amjcard.2010.07.038>

- [13] Watanabe, M., Yokoshiki, H., Mitsuyama, H., Mizukami, K., Ono, T. and Tsutsui, H. (2012) Conduction and Refractory Disorders in the Diabetic Atrium. *American Journal of Physiology-Heart and Circulatory Physiology*, **303**, H86-H95. <https://doi.org/10.1152/ajpheart.00010.2012>
- [14] Demir, K., Avci, A., Kaya, Z., Marakoglu, K., Ceylan, E., Yilmaz, A., *et al.* (2016) Assessment of Atrial Electromechanical Delay and P-Wave Dispersion in Patients with Type 2 Diabetes Mellitus. *Journal of Cardiology*, **67**, 378-383. <https://doi.org/10.1016/j.jcc.2015.06.003>
- [15] Kuehl, M. and Stevens, M.J. (2012) Cardiovascular Autonomic Neuropathies as Complications of Diabetes Mellitus. *Nature Reviews Endocrinology*, **8**, 405-416. <https://doi.org/10.1038/nrendo.2012.21>
- [16] Rizzo, M.R., Sasso, F.C., Marfella, R., Siniscalchi, M., Paolisso, P., Carbonara, O., *et al.* (2015) Autonomic Dysfunction Is Associated with Brief Episodes of Atrial Fibrillation in Type 2 Diabetes. *Journal of Diabetes and Its Complications*, **29**, 88-92. <https://doi.org/10.1016/j.jdiacomp.2014.09.002>
- [17] Ko, S.H., Park, Y.M., Yun, J.S., *et al.* (2018) Severe Hypoglycemia Is a Risk Factor for Atrial Fibrillation in Type 2 Diabetes Mellitus: Nationwide Population-Based Cohort Study. *Journal of Diabetes and its Complications*, **32**, 157-163. <https://doi.org/10.1016/j.jdiacomp.2017.09.009>
- [18] Fatemi, O., Yuriditsky, E., Tsioufis, C., Tsachris, D., Morgan, T., Basile, J., *et al.* (2014) Impact of Intensive Glycemic Control on the Incidence of Atrial Fibrillation and Associated Cardiovascular Outcomes in Patients with Type 2 Diabetes Mellitus (from the Action to Control Cardiovascular Risk in Diabetes Study). *The American Journal of Cardiology*, **114**, 1217-1222. <https://doi.org/10.1016/j.amjcard.2014.07.045>
- [19] Fiaschi, T., Magherini, F., Gamberi, T., Lucchese, G., Faggian, G., Modesti, A., *et al.* (2014) Hyperglycemia and Angiotensin II Cooperate to Enhance Collagen I Deposition by Cardiac Fibroblasts through a ROS-STAT3-Dependent Mechanism. *Biochimica et Biophysica Acta—Molecular Cell Research*, **1843**, 2603-2610. <https://doi.org/10.1016/j.bbamcr.2014.07.009>
- [20] Monnier, L., Mas, E., Ginet, C., Michel, F., Villon, L., Cristol, J., *et al.* (2006) Activation of Oxidative Stress by Acute Glucose Fluctuations Compared with Sustained Chronic Hyperglycemia in Patients with Type 2 Diabetes. *Journal of the American Medical Association*, **295**, 1681-1687. <https://doi.org/10.1001/jama.295.14.1681>
- [21] Staszewsky, L., Cortesi, L., Baviera, M., Tettamanti, M., Marzona, I., Nobili, A., *et al.* (2015) Diabetes Mellitus as Risk Factor for Atrial Fibrillation Hospitalization: Incidence and Outcomes over Nine Years in a Region of Northern Italy. *Diabetes Research and Clinical Practice*, **109**, 476-484. <https://doi.org/10.1016/j.diabres.2015.06.006>
- [22] Pallisgaard, J.L., Schjerning, A., Lindhardt, T.B., Procidia, K., Hansen, M.L., Torp-Pedersen, C., *et al.* (2016) Risk of Atrial Fibrillation in Diabetes Mellitus: A Nationwide Cohort Study. *European Journal of Preventive Cardiology*, **23**, 621-627. <https://doi.org/10.1177/2047487315599892>
- [23] Bhupathiraju, S.N. and Hu, F.B. (2016) Epidemiology of Obesity and Diabetes and Their Cardiovascular Complications. *Circulation Research*, **118**, 1723-1735. <https://doi.org/10.1161/circresaha.115.306825>
- [24] Tedrow, U.B., Conen, D., Ridker, P.M., Cook, N.R., Koplan, B.A., Manson, J.E., *et al.* (2010) The Long and Short-Term Impact of Elevated Body Mass Index on the Risk of New Atrial Fibrillation. *Journal of the American College of Cardiology*, **55**, 2319-2327. <https://doi.org/10.1016/j.jacc.2010.02.029>
- [25] Wang, T.J. (2004) Obesity and the Risk of New-Onset Atrial Fibrillation. *Journal of the American Medical Association*, **292**, 2471-2477. <https://doi.org/10.1001/jama.292.20.2471>
- [26] Scirica, B.M., Bhatt, D.L., Braunwald, E., Steg, P.G., Davidson, J., Hirshberg, B., *et al.* (2013) Saxagliptin and Cardiovascular Outcomes in Patients with Type 2 Diabetes Mellitus. *New England Journal of Medicine*, **369**, 1317-1326. <https://doi.org/10.1056/nejmoa1307684>
- [27] Saisho, Y. (2015) Metformin and Inflammation: Its Potential beyond Glucose-Lowering Effect. *Endocrine, Metabolic & Immune Disorders-Drug Targets*, **15**, 196-205. <https://doi.org/10.2174/1871530315666150316124019>
- [28] Wang, J., Zhu, L., Hu, K., Tang, Y., Zeng, X., Liu, J., *et al.* (2017) Effects of Metformin Treatment on Serum Levels of C-Reactive Protein and Interleukin-6 in Women with Polycystic Ovary Syndrome. *Medicine*, **96**, e8183. <https://doi.org/10.1097/md.00000000000008183>
- [29] Kume, O., Takahashi, N., Wakisaka, O., Nagano-Torigoe, Y., Teshima, Y., Nakagawa, M., *et al.* (2011) Pioglitazone Attenuates Inflammatory Atrial Fibrosis and Vulnerability to Atrial Fibrillation Induced by Pressure Overload in Rats. *Heart Rhythm*, **8**, 278-285. <https://doi.org/10.1016/j.hrthm.2010.10.029>
- [30] Buckingham, R.E. (2005) Thiazolidinediones: Pleiotropic Drugs with Potent Anti-Inflammatory Properties for Tissue Protection. *Hepatology Research*, **33**, 167-170. <https://doi.org/10.1016/j.hepres.2005.09.027>
- [31] Theofilis, P., Sigris, M., Oikonomou, E., Antonopoulos, A.S., Siasos, G., Tsioufis, K., *et al.* (2022) Pleiotropic Effects of SGLT2 Inhibitors and Heart Failure Outcomes. *Diabetes Research and Clinical Practice*, **188**, Article 109927. <https://doi.org/10.1016/j.diabres.2022.109927>
- [32] Theofilis, P., Antonopoulos, A.S., Katsimichas, T., Oikonomou, E., Siasos, G., Aggeli, C., *et al.* (2022) The Impact of

- SGLT2 Inhibition on Imaging Markers of Cardiac Function: A Systematic Review and Meta-Analysis. *Pharmacological Research*, **180**, Article 106243. <https://doi.org/10.1016/j.phrs.2022.106243>
- [33] Theofilis, P., Vordoni, A. and Kalaitzidis, R.G. (2022) Oxidative Stress Management in Cardiorenal Diseases: Focus on Novel Antidiabetic Agents, Finerenone, and Melatonin. *Life*, **12**, Article 1663. <https://doi.org/10.3390/life12101663>
- [34] Theofilis, P., Sagris, M., Oikonomou, E., Antonopoulos, A.S., Siasos, G., Tsioufis, K., *et al.* (2022) The Anti-Inflammatory Effect of Novel Antidiabetic Agents. *Life*, **12**, Article 1829. <https://doi.org/10.3390/life12111829>
- [35] Hankey, G.J., Jamrozik, K., Broadhurst, R.J., Forbes, S. and Anderson, C.S. (2002) Long-Term Disability after First-Ever Stroke and Related Prognostic Factors in the Perth Community Stroke Study, 1989-1990. *Stroke*, **33**, 1034-1040. <https://doi.org/10.1161/01.str.0000012515.66889.24>
- [36] Kirchhof, P., Benussi, S., Kotecha, D., Ahlsson, A., Atar, D., Casadei, B., *et al.* (2016) 2016 ESC Guidelines for the Management of Atrial Fibrillation Developed in Collaboration with EACTS. *European Heart Journal*, **37**, 2893-2962. <https://doi.org/10.1093/eurheartj/ehw210>
- [37] Patti, G., Lucerna, M., Cavallari, I., Ricottini, E., Renda, G., Pecun, L., *et al.* (2017) Insulin-Requiring versus Noninsulin-Requiring Diabetes and Thromboembolic Risk in Patients with Atrial Fibrillation. *Journal of the American College of Cardiology*, **69**, 409-419. <https://doi.org/10.1016/j.jacc.2016.10.069>
- [38] Patti, G., Cavallari, I., Andreotti, F., Calabrò, P., Cirillo, P., Denas, G., *et al.* (2019) Prevention of Atherothrombotic Events in Patients with Diabetes Mellitus: From Antithrombotic Therapies to New-Generation Glucose-Lowering Drugs. *Nature Reviews Cardiology*, **16**, 113-130. <https://doi.org/10.1038/s41569-018-0080-2>
- [39] Cheung, C., Sing, C., Lau, W.C.Y., Li, G.H.Y., Lip, G.Y.H., Tan, K.C.B., *et al.* (2021) Treatment with Direct Oral Anticoagulants or Warfarin and the Risk for Incident Diabetes among Patients with Atrial Fibrillation: A Population-Based Cohort Study. *Cardiovascular Diabetology*, **20**, Article No. 71. <https://doi.org/10.1186/s12933-021-01263-0>
- [40] Ebert, M., Stegmann, C., Kosiuk, J., Dinov, B., Richter, S., Arya, A., *et al.* (2017) Predictors, Management, and Outcome of Cardioversion Failure Early after Atrial Fibrillation Ablation. *EP Europace*, **20**, 1428-1434. <https://doi.org/10.1093/europace/eux327>
- [41] Abadie, B.Q., Hansen, B., Walker, J., Deyo, Z., Biese, K., Armbruster, T., *et al.* (2019) Likelihood of Spontaneous Cardioversion of Atrial Fibrillation Using a Conservative Management Strategy among Patients Presenting to the Emergency Department. *The American Journal of Cardiology*, **124**, 1534-1539. <https://doi.org/10.1016/j.amjcard.2019.08.017>
- [42] Handelsman, Y., Bunch, T.J., Rodbard, H.W., Steinberg, B.A., Thind, M., Bigot, G., *et al.* (2022) Impact of Dronedarone on Patients with Atrial Fibrillation and Diabetes: A Sub-Analysis of the ATHENA and EURIDIS/ADONIS Studies. *Journal of Diabetes and its Complications*, **36**, Article 108227. <https://doi.org/10.1016/j.jdiacomp.2022.108227>
- [43] Iervasi, G., Clerico, A., Bonini, R., Nannipieri, M., *et al.* (1998) Effect of Antiarrhythmic Therapy with Intravenous Loading Dose of Amiodarone: Evidence for an Altered Response in Diabetic Patients. *International Journal of Clinical Pharmacy*, **18**, 109-120.
- [44] Veglio, M., Bruno, G., Borra, M., Macchia, G., Bargero, G., D'errico, N., *et al.* (2002) Prevalence of Increased QT Interval Duration and Dispersion in Type 2 Diabetic Patients and Its Relationship with Coronary Heart Disease: A Population-Based Cohort. *Journal of Internal Medicine*, **251**, 317-324. <https://doi.org/10.1046/j.1365-2796.2002.00955.x>
- [45] D'Angelo, R.N., Rahman, M., Khanna, R., Yeh, R.W., Goldstein, L., Yadalam, S., *et al.* (2021) Limited Duration of Antiarrhythmic Drug Use for Newly Diagnosed Atrial Fibrillation in a Nationwide Population under Age 65. *Journal of Cardiovascular Electrophysiology*, **32**, 1529-1537. <https://doi.org/10.1111/jce.15012>
- [46] Kirchhof, P., Camm, A.J., Goette, A., Brandes, A., Eckardt, L., Elvan, A., *et al.* (2020) Early Rhythm-Control Therapy in Patients with Atrial Fibrillation. *New England Journal of Medicine*, **383**, 1305-1316. <https://doi.org/10.1056/nejmoa2019422>
- [47] Kim, M.H., Yu, H.T., Park, Y.J., *et al.* (2022) Diabetes Mellitus Is an Independent Risk Factor for a Stiff Left Atrial Physiology after Catheter Ablation for Atrial Fibrillation. *Frontiers in Cardiovascular Medicine*, **9**, Article 828478. <https://doi.org/10.3389/fcvm.2022.828478>
- [48] Wang, A., Truong, T., Black-Maier, E., Green, C., Campbell, K.B., Barnett, A.S., *et al.* (2020) Catheter Ablation of Atrial Fibrillation in Patients with Diabetes Mellitus. *Heart Rhythm O²*, **1**, 180-188. <https://doi.org/10.1016/j.hroo.2020.04.006>
- [49] Anselmino, M., Matta, M., D'ascenzo, F., Pappone, C., Santinelli, V., Bunch, T.J., *et al.* (2015) Catheter Ablation of Atrial Fibrillation in Patients with Diabetes Mellitus: A Systematic Review and Meta-Analysis. *Europace*, **17**, 1518-1525. <https://doi.org/10.1093/europace/euv214>