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Review

Hand grip strength and diabetic foot ulcers: A mini-review

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Abstract

This narrative mini-review article aimed to discuss the emerging association between hand grip strength (HGS) and diabetic foot ulcers (DFUs). HGS is related to muscle strength and conditions such as sarcopenia. However, it can be utilized as a confirmative evaluation test of sarcopenia after initial screening tools such as the SARC-F questionnaire. Diabetes mellitus (DM) seems to be related to sarcopenia and skeletal muscle mass loss. In this narrative mini-review article, it was demonstrated that older type 2 diabetes mellitus (T2DM) subjects with DFUs had a higher rate of low HGS, while low HGS was significantly related to the occurrence of DFUs. Additionally, HGS might be a significant predictor not only of wound healing but also of the overall survival of DFU subjects and the likelihood of amputation. Nevertheless, further studies are needed to enable definitive conclusions and suggest potential practical implications.

Keywords: hand grip strength, diabetes mellitus, diabetic foot, diabetic foot ulcers, sarcopenia.

Introduction

Hand grip strength measurement has gained attention as an easy, noninvasive marker of upper extremity muscle strength assessment, appropriate for everyday clinical utilization, among other muscle function techniques [1]. Low hand grip strength might be indicative of low muscle mass and sarcopenia, although there is notable variation in the existing procedures of evaluating grip strength, which makes comparison among studies hard [1–3].

Diabetic foot ulcers (DFUs) are a very frequent complication of long-standing diabetes mellitus (DM) related to increased amputation rates and mortality, while outcomes in DM and DFUs are already established to rely strongly on social determinants of health, with worse impact on minority and socioeconomically disadvantaged groups [4]. It is becoming increasingly recognized that subjects with DFUs frequently exhibit sarcopenia (loss of muscle mass and function) [5].

Thus, this narrative mini-review aimed to investigate the emerging interplay between DFUs and HGS.

Search strategy

We carried out online research in Google Scholar, PubMed and EMBASE from February 1997 until May 2024 using combinations of the following keywords: “hand grip strength” OR “hand grip” AND “diabetic foot” OR “diabetic foot ulcers”. Only original articles written in English were included, while references

concerning included studies were also investigated. (Figure 1, PRISMA flowchart diagram (http://www.prisma-statement.org).

Hand grip strength (HGS): a significant diagnostic and prognostic parameter

HGS is a simple diagnostic tool to assess the upper limb strength function in subjects with various diseases [6]. HGS seems to be the single evaluation technique proposed for assessing muscle strength and is the easiest procedure for evaluating muscle function in everyday clinical practice [1, 3]. HGS declines after midlife, with accelerating reduction with increasing age and through old age [3]. HGS appears to have predictive validity, and decreased values are related to disability, falls, impaired quality of life (QoL), increased duration of hospitalization and eventually increased mortality [3, 7]. HGS measurement can be conducted utilizing a HGS dynamometer [3]. The Jamar hand dynamometer (Lafayette Instrument Company, USA) is the most broadly cited in the existing literature and is known as the gold standard by which other kinds of dynamometers are assessed [3]. In addition, it has already been recorded that there might be a circadian rhythm in HGS, with a minimum value of around 06:00 h and a maximum of around 18.00 h [3].

A standard protocol utilized to measure adult hand grip strength is the Southampton protocol [3]. According to this protocol, the subject is seated comfortably in a specific chair with legs, fixed arms and back support, utilizing the same chair for every evaluation [3]. Following, the researcher asks subjects to rest their forearms on the arms of the chair with their wrist just over the end of the arm of the chair, and he/she demonstrates how to utilize the dynamometer to underly that gripping strongly leads to the optimum result, beginning with the right hand [3]. Moreover, the subject should be encouraged to position the hand so that the thumb is around one side of the handle and the four fingers are around the other side, while the dynamometer should feel pleasant in the subject's hand. It is of great importance that the researcher should rest the base of the dynamometer on the palm of his/her hand as the subject grabs the dynamometer to support the weight of the dynamometer, but without restricting its movement [3]. The subject should press as long and as tightly as possible or till the needle stops rising, where the researcher records the outcome to the nearest 1 kg. This measurement should be repeated in the left hand, while two further measurements for each hand are imperative to be carried out [3]. The best of the six grip strength results is utilized in statistical analyses, while the researcher should also examine hand dominance [3].

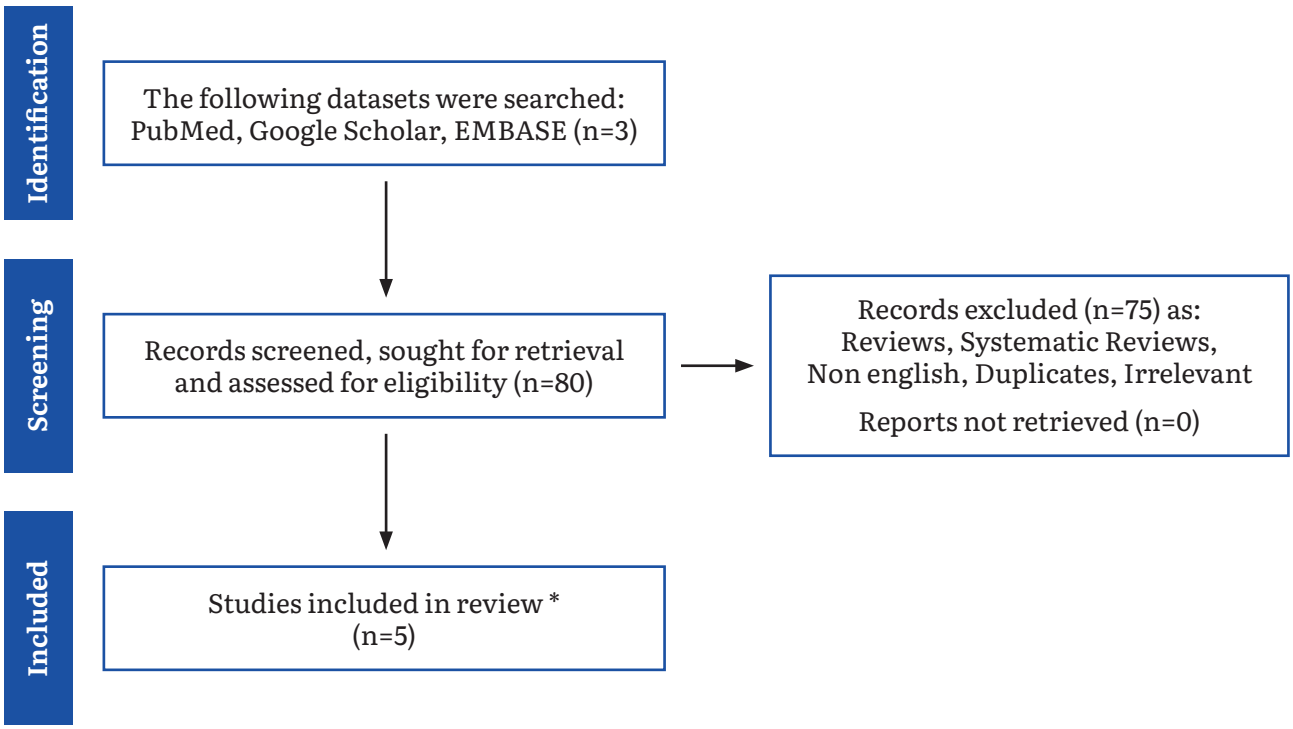

Figure 1: Flowchart diagram showing the literature review strategy. * – only original non-animal studies written in English were included.

In type 2 diabetes mellitus (T2DM), HGS is significantly related to mortality and cardiovascular disease (CVD) [8]. Moreover, it has been shown that higher fasting glucose was related to reduced HGS [9]. Importantly, T2DM may accelerate the development of sarcopenia, which is related to low HGS, through increased insulin resistance, accumulation of advanced glycation end-products, inflammation and oxidative stress [5, 10].

Importantly, HGS can be used as a biomarker of outcomes among older individuals, such as bone mineral density, nutritional status, comorbidity burden, cognitive function, emotional disorders and even hospitalization and mortality as already described [7, 11].

Diabetic foot ulcers (DFUs)

DFUs are a costly and serious complication of DM [12]. DFUs are related to significant morbidity and mortality, leading to increased hospitalization rates and lower limb amputation if not diagnosed and treated appropriately [13]. The investigation of any potential prognostic tool concerning the development of DFUs and their course remains a significant issue to explore among the scientific community. Given the fact that the underlying pathophysiology of DFUs is an intricate interplay among the body's persistent hyperglycemic status and neuropathic, vascular and immune system status, it is important that multidisciplinary and multi-professional teamwork is conducted [14, 15].

There are plenty of risk factors concerning the formation of DFUs, such as peripheral neuropathy, arterial insufficiency, foot distortion and callus formation, leading to the creation of high-pressure areas, autonomic neuropathy and dry skin, limited joint mobility, inadequate glucose control, obesity, history of DFUs and even inappropriate footwear [16].

To evaluate the risk and severity of DFUs, many inflammatory biomarkers have been used such as procalcitonin, pentraxin-3, C-reactive protein (CRP), interleukins (ILs), and tumor necrosis factor-α (TNF-α). However, to achieve better therapeutic interventions, additional biomarkers are important to validate, taking into consideration also genomics, proteomics, metabolomics and microbiome in the understanding and treatment of DFUs [17].

The latest International Working Group on Diabetic Foot (IWGDF) recommended the use of Site, Ischemia, Neuropathy, Bacterial Infection, and Depth Classification System, which records ulcer area, depth, ischemia, infection and denervation and therefore is easy to use [18]. Other well-established systems are the Wagner classification system, which records the ulcer's depth and presence of gangrene; the Perfusion, Extent, Depth, Infection, and Sensation (PEDIS) Classification System, which categorizes DFUs based on perfusion, extent/size, depth/tissue loss, infection and sensation and has shown good reliability, the Infectious Disease Society of America/IWGDF infection classification which concerns infected DFUs and consists of 4 grades and the WIfI (Wound, Ischemia, and foot Infection) score classification system, which was proposed by the Society of Vascular Surgery and concerns the risk of vascular intervention [18]. However, the Wagner classification system does not consider peripheral artery disease or infection and has concerns for consistency, whilst the PEDIS classification system was not developed for prognostic purposes [18].

Finally, a plethora of interventions have been suggested, including both surgical and nonsurgical solutions, in relation to the nonsurgical intervention's autolytic hydrogels, enzymatic debridement, oxygen therapies, negative pressure wound therapy, human growth factors, bioengineered skin substitutes, and energy-based therapies [18]. The control of various and serious diabetic foot (DF) complications requires the collaboration of different specialists to provide the optimum handling of multiple kinds of diabetes care. This team of specialists often consists of a diabetologist, microbiologist, tissue viability nurse, podiatrist, orthopedic surgeon and vascular surgeon with a rigorous comprehension of foot function [14]. In general, surgical debridement, lessening pressure from weight bearing, managing lower extremity ischemia and DF infection, and early referral for diabetes care are first-line treatments for DFUs [19].

Hand grip strength and diabetic foot ulcers: the emerging potential thrilling interplay

In this non-systematic literature review, we tried to evaluate and assess any potential association between DFUs and HGS according to the existing literature. Four studies provided us with intriguing results concerning the interplay of these two clinical entities.

Imre *et al.* investigated the prevalence of low HGS in older subjects with T2DM who have diabetic foot disease (DFD) and evaluated the interplay between HGS and DFD in older subjects with T2DM [20]. They included 89 geriatric subjects with DFUs and 69 subjects without DFUs, while the exclusion criteria were the utilization of steroids, myopathy, disability, stroke-induced

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quadriplegia, type 1 diabetes, hemodialysis treatment, subjects under 65 years of age, and history of malignancy. The Wagner score was utilized to assess the severity of DFUs, and HGS was measured with a portable digital dynamometer. The cut-off values for low HGS were <16 kg (kilograms) for females and <27 kg for males [20]. Overall, 49 subjects (55.1%) with DFUs and 25 (36.2%) subjects without DFUs had low HGS (p=0.019) [20]. DFU subjects with lower HGS had higher measurements of PAD compared to subjects with DFUs who had typical HGS (p=0.009) [20]. Additionally, DFU subjects with lower HGS exhibited importantly higher rates of Wagner scores 4 and 5 and lower rates of Wagner scores 1 and 3 (p=0.039) [20].

González-Colaço Harmand *et al.* [21] examined the deleterious effects of sarcopenia and malnutrition on DFUs healing, hospitalization and functional impairment among elderly subjects. In a prospective observational study, they included 45 T2DM subjects (71% men) aged 65–93 years (mean age 76.82±8.08 years). More than half of them (53.3%) had >10 years of T2DM duration [21]. All participants were evaluated at admission and at 3 months after coming back home to discover the quality of life (QoL), mobility and healing, pain, and overall hospital stay concerning the malnutrition presence and sarcopenia assessed by grip strength, among other syndromes of the elderlies. Overall, 29 subjects (64.4%) had previously experienced DFUs. HGS and sarcopenia were evaluated by a dynamometer [21]. Sarcopenia was diagnosed in 12 subjects (26.7%), whilst DF pain was evaluated using a 0–10 visual analog scale (VAS), with 10 representing the most acute pain [21]. Pain score was related to the presence of ischaemic heart disease (p=0.039), re-admissions (p=0.008) and sarcopenia (p=0.009). Nevertheless, subjects with complete ulcer healing had less pain at discharge (p=0.005), lower body-mass index (26.89±5.12 *vs.* 31.41±5.19 kg/m^2, p=0.011), better cognitive status (p=0.030), and slightly higher QoL at the beginning of the study (p=0.074) [21].

In a prospective observational study, Pena *et al.* [22] evaluated limb and subject factors related to key clinical outcomes in 152 DFU subjects. Diabetic subjects with foot ulcers were admitted to a major tertiary teaching hospital in South Australia or evaluated at multidisciplinary foot clinics between February 2017 and December 2018, while subjects' demographic and clinical data were recorded, including limb status severity evaluated by the WIfI system and HGS, with a follow-up period of the participants up for 12 months. Of these, 42 underwent revascularisation during the time of the study, while 18 (11.8%) sustained important amputation of the index limb, and 16 (10.5%) passed away until re-examination [22]. Complete wound healing was achieved in 106 (70%) participants [22]. Subjects with low HGS appeared to be 50% less likely to reach wound healing than subjects with sufficient grip strength [22]. For every one unit increase in Wound, Ischemia, and foot Infection (WIfI) stage, the sub-distribution hazard of major amputation increased 2.75 times (hazard ratio [HR]: 2.75, 95% confidence interval [CI]: 1.10–6.88, p=0.031), the hazard of dying increased by 2.60 times (HR: 2.60, 95% CI 1.19–5.69, p=0.016), the sub-distribution hazard of healing decreased by 31% (HR: 0.69, 95% CI 0.57–0.84, p<0.001) and the odds of having amputation free survival reduced by 68% (OR 0.32, 95% CI: 0.17–0.61, p<0.001). A significant correlation of HGS with time to healing and with previous amputations (major or minor) was additionally recorded [22].

López-Valverde *et al.* examined the hypothesis that subjects with malnutrition and deteriorated muscle function determined by HGS might have adverse outcomes [23]. They carried out a prospective observational study and included 77 subjects admitted for ischemic DFUs and examined any potential adverse effects of malnutrition and reduced HGS. Global Leadership Initiative on Malnutrition (GLIM) criteria were used to diagnose malnutrition. HGS measurements extracted from a dynamometer were dichotomized into < and ≥ mean, depending on the measurements acquired in both sexes [23]. Totally, 55 subjects (71.4%) had insufficient levels of nutrition. Malnutrition was not related to any adverse outcome. Meanwhile, HGS < mean was related to the subject's age, DM duration, body-mass index, plasma albumin, prealbumin, brachial circumference, transferrin, hemoglobin and HbA1c [23]. Importantly, prognostic variables of mortality (multivariate Cox model) were age more than 69 years (hazard ratio [HR]: 4.0, 95% confidence interval [CI]: 1.3–12.0, p=0.01), and HGS < mean (HR: 3.7, 95% CI 1.2–11.3, p=0.01). Survival time in subjects with HGS < mean was lower compared to those with HGS ≥ mean (p<0.01) [23].

Imre *et al.* investigated and analyzed the prognostic importance of HGS as a predictor of lower extremity amputation at 1-year follow-up in subjects with T2DM. [24]. They evaluated 526 subjects with T2DM, whilst HGS was evaluated utilizing a handheld Smedley digital dynamometer following the NHANES Muscle Strength/Grip Test Procedure. (ref) Low HGS was defined for women as less than 16 kg and for men less than 27 kg [24]. Overall, a total of 205 subjects were utilized for this study. Subjects' mean age was 59 years old, 37% were women, and the mean DM disease duration was

14 years [24]. Seventy-seven (37%) subjects sustained lower extremity amputations (26 major and 51 minor amputations). This study demonstrated after controlling for age, presence of peripheral artery disease, body mass index (BMI), gender and white cell counts (WBC) as confounded variables, that subjects with low HGS had an augmented hazard for amputations (OR: 2.17; 95% CI: 1.09–4.32; p<0.001) [24].

The type and the design of studies, the under-investigation population and the main results of the abovementioned studies are all presented in Table 1.

Discussion

This narrative mini review has demonstrated that low HGS might be a predictor of impaired healing and of poor prognosis in DFUs patients. Furthermore, low HGS could be related to the occurrence of DFUs. Nevertheless, it is significant that we try to explain these results based on the existing literature and knowledge.

The abovementioned association may be explained by the fact that HGS is an objective test of muscle strength and, hence, of sarcopenia [3, 25]. The latter is now known to be common in DM and associated with diabetic complications [26, 27]. In this context, Argilés *et al*. [28] have proposed that decreased muscle mass leaves subjects without a significant reservoir of amino acids, cytokines and myokines released by muscle, thereby reducing the ability to fight illness and infection [28]. This mechanism could, at least partly, explain the adverse outcomes in DFU subjects with low HGS and reduced muscle mass. Certainly, reduced muscle mass may predispose to injury, increasing the risk of DFUs [29, 30].

HGS measurement is a fast, not expensive, and non-invasive assessment which can be easily carried out in internal and external hospitalized individuals, requiring marginal training and portable, cheap equipment and therefore it might be useful in everyday clinical practice [22]. Given the fact that subjects with DFUs have a higher danger of re-ulceration, a clear protocol for HGS evaluation is imperative to confirm its trustworthiness [22].

It would be of great interest if we could investigate if there is any specific cutoff value of hand grip strength in which the prognosis of DFUS in DM subjects seems to be significantly poor and adverse outcomes might be imminent [24]. In addition, it would be quite interesting if we could assess and record which kind of the existing HGS dynamometers, such as hydraulic and mechanic dynamometers, could provide us the optimum results concerning grip strength measurement specific in DM subjects suffering from DFUs. This means that various comparative multicentre studies with a large number of participants should be carried out to record any differences among different types of HGS dynamometers.

Another important issue that should be addressed is whether ameliorating hand grip strength might have a positive impact on wound healing and whether there are specific and more beneficial than already recorded interventions, especially for DM subjects who suffer from DFUs. Among these interventions that should be investigated are nutritional and training interventions since DM subjects might have certain restrictions based on the medical issue that they confront. A group of specific scientists, such as dietitians, physical fitness experts, and trainers, should engage in this intriguing and quite interesting interplay. The collaboration of various specialties could provide DFU patients with the best approach to their issues. Nevertheless, it seems imperative that this group of physicians and scientists should be well-trained and aware of these two clinical entities. Along with these scientists, subjects suffering from DFUs should also be aware of the concept of sarcopenia, low HGS and skeletal muscle mass health. This means that everyday physicians should inform properly and thoroughly subjects with DFUs concerning skeletal muscle mass health and propose a measurement of HGS as an initial measurement. It is already recorded that specific screening tools such as the SARC-F questionnaire, which is a questionnaire consisting of five parameters strength (S), assistance walking (A), rising from a chair (R), climbing stairs (C), and falls (F) on a scale of 0 to 2, with a cutoff value ≥4 points, can provide us with valuable information concerning a subject's skeletal muscle mass status in order to further proceed to HGS measurement [31].

It should be mentioned that the constraints of current knowledge are related to the reduced number of studies. It seems that only observational studies, including small participant numbers, are currently available, minimizing their level of evidence. Thus, additional larger prospective studies are needed. In addition, studies deriving from various medical centers all around the world recruiting different kinds of populations from different races, ages, and social levels could provide us with significant information, and such works may help us draw definitive conclusions.

Conclusion

In this narrative mini-review article, it was demonstrated that low HGS might be a predictor of impaired

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Table 1: Association between HGS and DFUs.

Author [ref]	Study design	Study population	Main results
Imre *et al.* [20]	Single-center cross-sectional observational study	89 geriatric T2DM subjects with DFUs and 69 subjects without DFUs	49 subjects (55.1%) with DFUs and 25 (36.2%) subjects without DFUs had low HGS (p=0.019). DFU subjects with lower HGS had higher rates of PAD than subjects with DFUs with normal HGS (p=0.009). DFUs subjects with lower HGS had importantly higher rates of Wagner scores 4 and 5 and lower rates of Wagner scores 1 and 3 (p=0.039)
González-Colaço Harmand *et al.* [21]	Prospective observational study	45 subjects over 65 years with T2DM and DF	12 subjects (26.7%) were sarcopenic. Pain score was associated with the presence of ischaemic heart disease (4.27±3.24 *vs.* 2.46±1.98, p=0.039), readmissions (6.29±3.50 *vs.* 3.09±2.58, p=0.008) and sarcopenia (5.89±2.47 *vs.* 3±2.83, p=0.009). Nevertheless, subjects with complete ulcer healing had less pain at discharge (1.85±2.38 *vs.* 4.58±2.87; p=0.005)
Pena *et al.* [22]	Prospective observational study	153 subjects were recruited, and outcome data were obtained for 152	Complete wound healing was achieved in 106 (70%) subjects. There were significant associations between the WIfI stage and major amputation (SHR: 2.75), mortality (HR: 2.60), amputation-free survival (OR: 0.32), and wound healing (SHR 0.69). Statistically significant relation between time to healing and HGS (SHR 0.50) and previous amputations (major or minor) (SHR 0.57)
López-Valverde *et al.* [23]	Prospective observational study	77 subjects admitted for IDFU	55 subjects (71.4%) were malnourished. Malnutrition was not associated with adverse outcomes. HGS < mean was related to patient age, duration of DM, body mass index, plasma albumin, prealbumin, brachial circumference, transferrin, hemoglobin and HbA1c. Predictive variables of mortality were age >69 years (HR: 4.0, 95% CI: 1.3–12.0, p=0.01) and HGS < mean (HR: 3.7, 95% CI: 1.2–11.3, p=0.01). Survival time in subjects with HGS < mean was shorter than in those with HGS ≥ mean (p<0.01).
Imre *et al.* [24]	Prospective study	205 T2DM subjects	The subjects' mean age was 59 years old, 37% were women, and the mean duration of DM disease was 14 years. (ref) Seventy-seven (37%) subjects sustained lower extremity amputations (26 major and 51 minor amputations). Subjects with low HGS had an augmented hazard for amputations (OR: 2.17; 95% CI: 1.09–4.32; p<0.001)

Note: T2DM – type 2 diabetes mellitus; DFUs – diabetic foot ulcers; HGS – hand grip strength; p – p-value; PAD – peripheral artery disease; DF – diabetic foot; WIfI – wound, ischemia, and foot Infection; SHR – sub-distribution hazard ratio; HR – hazard ratio; OR – odds ratio; IDFU – ischemic diabetic foot ulcers; GLIM – Global Leadership Initiative on Malnutrition; CI – confidence interval.

healing and poor prognosis in DFU patients. Furthermore, low HGS could be connected to the occurrence of DFUs. Nevertheless, additional research is important to be conducted to enable definitive conclusions and suggest potential practical implications. It seems that these two entities have an intriguing connection, but scientists should dive into this upcoming interaction and collaboration among different specialties, which seems to be imperative for better understanding and management.

Conflict of interest

N. Papanas has been an advisory board member of Astra-Zeneca, Boehringer Ingelheim, MSD, Novo Nordisk, Pfizer, Takeda and TrigoCare International; has participated in sponsored studies by Astra-Zeneca, Eli-Lilly, GSK, MSD, Novo Nordisk, Novartis and Sanofi-Aventis; has received honoraria as a speaker for Astra-Zeneca, Boehringer Ingelheim, Eli-Lilly, ELPEN, Galenica, MSD, Mylan, Novo Nordisk, Pfizer, Sanofi-Aventis, Takeda and Vianex; and attended conferences sponsored by TrigoCare International, Eli-Lilly, Galenica, Novo Nordisk, Pfizer and Sanofi-Aventis.

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