Cardiac autonomic neuropathy (CAN) is a complication of diabetes mellitus, which imposes significant functional limitations and at times, sudden death. In an evolving healthcare landscape, physical therapists are assuming greater clinical responsibility and thus must be aware of this potential complication and tailor the plan of care appropriately. The purpose of this case report is to highlight the need for increased awareness of CAN among physical therapists in order to improve screening, diagnosis, and treatment. A 41-year-old Spanish-speaking male with uncontrolled type 2 diabetes arrived to the emergency department (ED) with dizziness and syncope leading to an inability to walk, work, or complete community service hours. After evaluation by the ED physical therapist, the patient was admitted for further work-up and diagnosed with CAN. After a short hospital course, the patient returned home symptomatic, fell, and was re-admitted the same day. Throughout the second hospital stay, the patient’s symptoms improved with robust medical management allowing physical therapy treatment and functional independence for safe discharge home. Additionally, patient-specific goals were met with the help of social work and the medical team. Clinical knowledge of CAN for the non-cardiopulmonary specialist physical therapist is lacking. As physical therapists prepare to be advanced practice providers in a rapidly evolving healthcare landscape, increasing awareness has the potential to lead to improved screening, diagnosis, and treatment of persons with CAN, a severe complication of diabetes.

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mortality rate, with a relative risk of 3.65 and 6.2 as reported in separate meta-analyses (Agashe and Petak, 2018; Spallone et al., 2011; Vinik et al., 2013; Maser et al., 2003; Vinik and Ziegler, 2007). The presence of CAN increases with length of disease; it is hypothesized that up to 60% of persons having type 2 diabetes for at least 15 years may present with symptoms of CAN (Pop-Busui et al., 2017).

When evaluating for CAN, common differentials include but are not limited to: peripheral vascular syndromes, various other central neurological diagnoses, genitourinary syndromes, metabolic syndromes, and cardiorespiratory diseases (Balcıoglu and Müderrisoğlu, 2015). However, the gold standard for the diagnosis of CAN are cardiovascular autonomic reflex tests (CARTs), also known as Ewing’s battery, developed by Ewing and Clarke in the 1970s (Serhiyenko and Serhiyenko, 2018; Spallone et al., 2011; Duque A et al., 2021). These five bedside tests assess sympathetic and parasympathetic cardiac function in persons with suspected CAN (Andersen et al., 2018); they are sensitive, specific, reproducible, standardized, and should be performed by medical practitioners trained in their implementation (Table 1) (Spallone et al., 2011a,b). Because of its clinical and prognostic significance and ease of applicability, the orthostatic hypotension test (Spallone et al., 2009) should be applied yearly by all medical practitioners in persons with diabetes, regardless of the presence of symptoms (Spallone et al., 2011). In this test, the patient’s blood pressure is measured after 5 minutes in supine and again after 1 and 2 minutes of standing and is considered abnormal if there is a systolic decrease >30 mmHg between the supine and the lowest standing value (Spallone et al., 2011a,b). The presence of one positive CART’s test indicates a possible diagnosis whereas two positive tests are needed for a definitive diagnosis (Serhiyenko and Serhiyenko, 2018; Spallone et al., 2011). Diagnosis criteria is based on the strong association between CAN and risk of mortality: in the presence of one abnormal CART the pooled relative risk is 1.20 (1.02–1.41; P = 0.03), in the presence of 2 or more abnormal tests the pooled relative risk is 3.45 (95% CI 2.66–4.47; P < 0.001) (Maser et al., 2003). The presence of orthostatic hypotension in addition to any one positive CARTS test indicates severe disease (Serhiyenko and Serhiyenko, 2018; Maser and Lenhard, 2005). The feasibility of CART’s tests has recently been called into question and more up-to-date tools such as nuclear imaging are under consideration as this may increase the sensitivity of CART’s (Duque et al., 2021). When using myocardial scintigraphy as a reference standard a cutoff score of two or more abnormal CART’s tests proved highly sensitive in the diagnosis of CAN (Sn 100%, Sp 33%) (Didangelos et al., 2018). In the absence of CART’s testing, CAN is a diagnosis of exclusion (Vinik et al., 2013; Balcıoglu and Müderrisoğlu, 2015). Because CAN is often mis-diagnosed, the importance of diagnosis must be overstated (Spallone et al., 2011). A clinical diagnosis of CAN allows the implementation of timely and possibly life-sparing therapies, enhances provider and patient motivation to correct glycemic abnormalities and cardiac risk factors and provides necessary information for disease management, such as the safe implementation of exercise (Boulton et al., 2005).

To date, no consensus nor evidence-based treatment algorithm exists for CAN (Serhiyenko and Serhiyenko, 2018). Treatment is multifaceted and interdisciplinary and includes nutrition and lifestyle changes in addition to medication management with emphasis on glycemic control and modification of cardiac risk factors (Serhiyenko and Serhiyenko, 2018; Vinik et al., 2013). If orthostatic hypotension is present, non-pharmacological interventions such as fluid volume replacement, liberal salt intake and compression wear are used in conjunction with pharmacological care. Slowly titrated sympathomimetics are the first drugs of choice in the management of orthostatic hypotension (Serhiyenko and Serhiyenko, 2018).

Physical therapists across all settings must be able to screen and treat persons with CAN (Lebec and Jogodka, 2009; Vinik et al., 2013). Although changes in state practice acts have expanded the scope of direct access to physical therapy (Garrity et al., 2020; Magel et al., 2020; Hon et al., 2021), variability remains (American Physical Therapy Association, 2016). Some states allow unrestricted direct access, that is the evaluation and management of patients without a physician referral, while others allow provisional or limited direct access (American Physical Therapy Association, 2016; Mabry et al., 2020). Physical therapists have successfully acted as advanced practice providers in the United States military for many decades (McLean, 2006; Mabry et al., 2020; Greathouse et al., 1994), evaluating and managing patients without a physician referral, ordering imaging and prescribing medication, performing thrust manipulations, and dry needling (Mabry et al., 2020). However, this broad scope of practice remains elusive in civilian settings (Mabry et al., 2020). For instance, physical therapists employed in emergency departments (ED) are prohibited by federal law from providing triage and initial medical evaluation (Centers for Medicare and Medicaid Services, 2021) and consultation of the ED PT occurs only after clearance from the referring ED provider (Matfat et al., 2019; Kim et al., 2018). However, this physician-centric model is expected to change (McLean, 2006; Mabry et al., 2020; Hon et al., 2021). In light of projected physician shortages (American Academy of Medical Colleges, 2021) and rising healthcare costs (Dieleman et al., 2017) physical therapists must be

| Table 1 Cardiovascular autonomic reflex tests (Agashe and Petak, 2018; Serhiyenko and Serhiyenko, 2018; Spallone et al., 2011; Paffili et al., 2015). |
|----------------------------------------|-----------------------------------|------------------------------------------|
| Test                                   | Administration                    | Response                                 |
| Deep breathing heart rate test (Sn 19%, Sp 98%, PPV 88%, NPV 57%, OR 2.34) | Patient supine, patient maximally breathes in and out 6 breaths per minute with use of metronome. Heart rated is monitored via EKG. | Normal response: Difference in heart rate >15 bpm. Abnormal response: A difference in heart rate <10 bpm. |
| Lying to standing heart rate test (Sn 96%, Sp 65%, PPV 72%, NPV 95%, OR 44.07) | With continuous EKG monitor: Measure R-R interval at beats 15 and 30 after rapid standing from supine position | Result is expressed by the 30:15 ratio. Longest R-R interval to the shortest R-R interval ratio after standing up. Normal is > 1.03, borderline is 1.01–1.03 Longest R-R interval to the shortest R-R interval ratio with maximal expiration. Normal is > 1.2, borderline is 1.11–1.2 |
| Valsalva maneuver heart rate test (Sn 62%, Sp 92%, PPV 76%, NPV 85%, OR 18.56) | With continuous EKG monitor: Patient forcefully exhales into manometer to 40mmHg for 15 seconds. Measure longest and shortest R-R intervals Measure systolic BP of patient in supine and after 1 and 2 minutes of standing. The last BP taken in supine is compared with the lowest value in standing. Establish maximum handgrip on dynamometer. Patient squeezes hand dynamometer at 30% maximum for 5 minutes. | Typical response is fall in systolic of <10 mmHg, borderline is fall of 10–29 mmHg, and abnormal is fall of >30 mmHg Typical response for diastolic BP is a rise of >16 mmHg on contralateral arm, borderline is 11–15 mmHg |

Abbreviations: EKG, electrocardiogram; bpm, beats per minute; mmHg, millimeters mercury; BP, blood pressure.
The following case underscores the role of the physical therapist in the medical care of a person with CAN, as well as accentuates the perils of failure to recognize this type of neuropathy. Although this case takes place in a physician-centric model of care, its lessons can be extended to all physical therapists preparing to be advanced practice providers in a rapidly evolving healthcare landscape. Thus, the purpose of this case report is to highlight the need for physical therapists’ awareness regarding the screening, diagnosis, and treatment of CAN, a severe complication of diabetes.

2. Case description

A 41-year-old Spanish-speaking male with a past medical history of hypertension, hyperlipidemia, and type 2 diabetes mellitus presented to the emergency department (ED) with complaints of dizziness and syncope for 8 months. His last medical follow-up was one year prior, during which his hemoglobin A1c was 12.5%. It is unknown if he adhered to his listed daily medications, which included: insulin, pravastatin, and lisinopril. Per chart review, multiple provider notes mention that patient frequently confused his medication dosing. The ED work up was notable for hyperglycemia, with a point-of-care glucose of 262 mg/dL, and tachycardia at rest as well as a normal chest x-ray, head computed tomography, basic metabolic panel, complete blood count and thyroid stimulating hormone. The ED physician referred the patient to the ED staff PT for a safety evaluation and with the expectation that the ED PT would provide disposition recommendations or request further assessment if warranted (Ferreira et al., 2018).

During the initial interview with the PT, the patient reported syncopal episodes multiple times a week, dizziness with upright postures, and syncope upon near-standing leading to an inability to walk or work construction. He maintained independence with activities of daily living as long as he was sitting or walking in a crouched position, including navigating stairs to his basement living quarters. He denied any red flags, as well as alcohol, tobacco or illicit drug use. He explained that, six months prior, he was found by police parked on the roadside slouched over his steering wheel due to worsening symptoms and was cited for drunk driving after being unable to fully stand to complete sobriety testing. As an undocumented person, he was sent to an immigration center for 6 months before being able to post his bond. His goal for the ED visit, therefore, was to provide his probation of sobriety testing and pass out of the hospital. In supine position, tests performed to rule out central and peripheral vestibular causes of dizziness were unremarkable. He ambulated with dizziness, maintaining a crouched position, while holding
items for stability. Vitals demonstrated orthostatic hypotension (fall in systolic \( \geq 30 \) mmHg), and fixed tachycardia (Table 2). The ED physical therapist determined that symptoms were attributable to a systemic dysfunction of unknown etiology. Due to pre-syncopal symptoms, unstable vitals, and orthostatic hypotension, the ED physical therapist deemed the patient unsafe for discharge home and referred the patient back to the emergency medicine physician recommending further workup (Table 3).

The patient remained in the ED for further observation and symptom control. He received 6L of intravenous fluids over a 48-h period, but was eventually admitted due to ongoing symptomatic orthostatic vitals. On the day of admission, neurology, cardiology, endocrinology, and internal medicine teams diagnosed CAN based off of exclusion of various other diseases and the presence of severe orthostatic hypotension with uncontrolled diabetes mellitus. The medical team then initiated sympathomimetics and insulin titration, recommended liberal caffeine and salt intake, hydration, and advised rising slowly. On hospital admission day one, PT evaluated the patient but deferred ambulation due to unstable vitals; he was, however able to transfer bed to chair with stand-by assistance. On hospital admission day two, the medical team entered their discharge summary and during physical therapy treatment the patient performed wheelchair mobility 300 feet independently with complaints of dizziness. The PT recommended the patient discharge home at wheelchair level with intermittent assistance as needed. Five days after the initial ED visit, on hospital admission day three, the patient discharged home symptomatic, with assistive devices to maximize safety, but without needed medical/legal paperwork (Table 4).

3. Outcomes

Six hours after discharge, the patient returned to the ED reporting syncope upon standing, in spite of rising slowly as
et al., 2017). Although the present case study depicts a male 
(coagulopathy, 2015). Additionally, the physical therapist
previously instructed. The patient was re-admitted to the hospital
where the medicine teams titrated sympathomimetics daily with
close monitoring and re-consulted physical therapy. On hospital re-
admission day one inpatient physical therapy deferred evaluation
due to unstable vitals. During the physical therapy evaluation on
hospital re-admission day two the patient demonstrated ongoing
orthostatic hypotension leading to the inability to ambulate. During
physical therapy on re-admission day four the patient tolerated
2 min of standing with dizziness, orthostatic vitals, and near syn-
cope. The next day the patient walked 400 feet independently and
negotiated seven steps over the course of two separate therapy
sessions with dizziness, but no syncope. On readmission day six,
the patient was discharged home asymptomatic with all necessary
medical paperwork for pending legal proceedings and adjusted
medications; he was able to safely ambulate and negotiate stairs
(Table 4).

4. Discussion

Physical therapists should tailor the medical screening portion
of their examination with persons at risk for CAN so as not to
overlook this common complication of diabetes. In particular, per-
sons with type 2 diabetes with a history of poor glycemic control
(hemoglobin A1c >7%), and/or cardiac risk factors require focused
inquiry (Agashe and Petak, 2018; Spallone et al., 2011; Pop-Busui
et al., 2017). Although the present case study depicts a male
patient, the literature does not suggest that sex is an increased risk
factor for CAN (Kempler et al., 2002). The physical therapist should
inquire about common symptoms of CAN such as lightheadedness,
dizziness, visual impairment, weakness or syncope. Medicine initiates
sympathomimetics and insulin titration of sympathomimetics and
insula. (Spallone and Ziegler et al., 2011; Andersen et al., 2018; Balc
es, 2018). When working with patients with CAN-induced orthostatic
hypotension, physical therapists in the inpatient setting should be aware that, with failure of non-pharmacological interventions, treatment of orthostatic
hypotension is entirely dependent on the administration of slowly titrated sympathomimetic medications until symptoms stabilize (Agashe and Petak, 2018). Then, to optimize safety prior to discharge home, physical therapists should progress patients with orthostatic hypotension from recumbent to upright exercise forms, ensuring tolerance to all functional positions (Serhiyenko and Serhiyenko, 2018; Pop-Busui et al., 2017). Considering the case at hand, the physical therapy team upon re-admission carefully considered patient orthostatic vitals and symptomatology during evaluation and treatment, ensuring a safe progression of movement and tolerance to all functional positions before clearing for discharge home. In contrast, during initial hospitalization, a lack of knowledge of CAN management and treatment led to an apparently premature discharge at wheelchair level, despite the patient’s specific needs to stand, walk, navigate stairs, work, and complete community service hours. Arguably, the aforementioned knowledge deficits jeopardized the PT’s clinical recommendations leading to inadvertent consequences: a preventable fall, a hospital re-admission, and unmet patient-specific goals (Table 4).

Physical therapists should consider the following general

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**Table 5**
Proposed decision-making tree for physical therapists in non-physician-centered facilities.
guidelines when treating persons with CAN. Ensure symptomatic patients, with or without abnormal CARTs, are up-to-date with recommended annual CARTs testing to evaluate for disease progression (Spallone et al., 2011). Preliminary evidence suggests aerobic exercise may improve glycemic control, cardiorespiratory fitness and autonomic function in persons with CAN (Bhati et al., 2018; Röhling et al., 2017). However, little else is known on the efficacy of exercise mode or training parameters (Bhati et al., 2018). Therefore, avoid implementing any exercise routine above functional baseline in patients with suspected or known disease until receipt of cardiovascular clearance including an exercise stress test (Serhiyenko and Serhiyenko, 2018; Spallone et al., 2011). Monitor exercise intensity using the heart rate reserve method or rate of perceived exertion (Röhling et al., 2017; Serhiyenko and Serhiyenko, 2018). Educate on the risks of exercise in extreme environments (eg heat or cold), rebound hypotension after high intensity exercise, and the benefits of aerobic exercise to minimize disease progression (Bhati et al., 2018; Serhiyenko and Serhiyenko, 2018; Agashe and Petak, 2018). Because joint manipulation and dry needling have a known effect on autonomic nervous system activity, physical therapists should exert caution and consider severity and stability of disease when utilizing these techniques (Sillevis et al., 2021; Picciottino et al., 2019; Savva et al., 2014). To date there are no studies evaluating these techniques in persons with CAN. Unfortunately, as pertains to this case, the patient was not offered outpatient physical therapy in spite of persistent functional incapacity with work and probation-related activities. It appears outpatient was not suggested due to a lack of awareness and knowledge surrounding physical therapy treatment efficacy and CAN.

Given the rise of the diabetes epidemic and in light of an evolving healthcare landscape, CAN is no longer a problem reserved for the cardiorespiratory specialist, but must be familiar to the entire healthcare team. In preparation for their role as advanced practice providers, it is imperative that physical therapists across the continuum of care obtain a more thorough understanding of CAN for the purposes of differential diagnosis and medical referral for timely and accurate diagnosis (Spallone et al., 2011) as well as safe and effective treatment implementation in a population at high risk for disease progression and sudden death (Boulton et al., 2005; Maser et al., 2003; Vinik and Ziegler, 2007). Future research could assess the impact of physical therapy-specific treatments on quality of life in persons with CAN, the development of CAN-specific functional outcome measures, and the efficacy of mode and exercise guidelines on CAN disease progression.

Clinical relevance

• In an evolving healthcare system, physical therapists across all settings must have greater awareness of CAN for improved patient-centered outcomes.

• Physical therapists may immediately implement screening and management strategies for CAN after learning clinical tests and treatment guidelines.

Patient consent

Patient written consent obtained and retained by the author.

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Declaration of competing interest

Germaine Herman and Sara Zehr are part-time employees at Eskenazi Health. The remaining authors have no conflicts of interest to declare.

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