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Viscerosomatic reflexes result in somatic dysfunction, which manifests as palpatory TART changes. There are two hypotheses of this study: palpatory findings will be associated with diabetes and will be associated with renal disease. An osteopathic predoctoral fellow conducted a palpatory exam on each subject at the level of T_{10}-L_2, to feel for TART changes. The results from the palpatory exam were recorded in SPSS for statistical analysis. Descriptive statistics, chi square and risk assessment were conducted. There were no statistically significant findings. Results demonstrated possible associations between type 2 diabetes mellitus and race, and tissue texture changes with control groups. Restriction of motion was found to have no difference amongst control and disease groups.

THE USE OF OSTEOPATHIC PALPATORY FINDINGS IN SCREENING FOR NEPHROPATHY IN TYPE 2 DIABETES MELLITUS:

A PILOT STUDY

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CHAPTER I

BACKGROUND AND SIGNIFICANCE

Type 2 Diabetes Mellitus

Diabetes mellitus is one of the commonest diagnoses in the United States. Each year the incidence of type 2 diabetes mellitus increases. In 2005, 1.5 million new cases of diabetes mellitus were diagnosed in the United States, with a total of 20.8 million individuals with diabetes.[1]

Type 2 diabetes mellitus was once thought of as 'adult onset diabetes', but physicians are now diagnosing type 2 diabetes mellitus more and more frequently in younger individuals, namely children as early as 9-10 years of age. The term non-insulin dependent diabetes mellitus is also being phased out as physicians and researchers learn more about the disease and its long term effects. Type 2 diabetes mellitus is currently defined as insulin resistance with an insulin secretory defect.[2] As opposed to type 1 diabetes mellitus where insulin is not being produced, in type 2 diabetes mellitus the pancreas is fully functioning and secreting insulin. But the glucose load is so great that the body progressively develops insulin resistance until finally the pancreas shuts down.[1] As a result, management of type 2 diabetes mellitus focuses on reduction of glucose load through diet, exercise, and education. Treatment also includes enhancement of insulin

production and function through the use of medications. Understanding diabetes mellitus is important in order to accurately screen, diagnose, and treat people who are at risk and who have diabetes.

With the prevalence of diabetes mellitus increasing, it is important to understand who is most at risk of developing the disease. Risk factors for type 2 diabetes mellitus include but are not limited to obesity, family history, older age, history of gestational diabetes, physical inactivity, race/ethnicity, and impaired fasting glucose.[1] The two most significant non-modifiable risk factors are gender and race. More men are affected by diabetes than women, with 10.5% of men with the disease as compared with 8.8% of women.[1] Non-white individuals are typically more affected with type 2 diabetes mellitus than white individuals. Non-Hispanic blacks and Hispanics are 1.8 and 1.7 times as likely to develop diabetes mellitus as non-Hispanic whites.[1] Identifying risk factors allows medical professionals to accurately screen patients who are more apt to develop type 2 diabetes mellitus.

Screening individuals for type 2 diabetes mellitus is recommended for those who are at risk. It is not recommended to screen people who are asymptomatic without any risk factors. Physicians monitor patients' blood glucose levels to screen for possible diabetes mellitus. The term "prediabetes" has been used to refer to individuals who have impaired fasting glucose (100-125 mg/dl) or who have impaired glucose tolerance (140-199 mg/dl).[2]

Diagnosing diabetes can be done with either the fasting glucose level or the oral glucose tolerance test (OGTT). The OGTT is the most sensitive test and is the gold

standard, but the fasting plasma glucose is typically recommended because it is easier to use, more acceptable to patients, and is not as costly.[2] The criteria for diagnosis includes the following: symptoms of diabetes (polyuria, polydipsia, and unexplained weight loss) and nonfasting glucose ≥ 200 mg/dl, or fasting plasma glucose ≥ 126 mg/dl, or OGTT ≥ 200 mg/dl.[2] Once a diagnosis of type 2 diabetes mellitus is made, the subsequent treatment of the disease focuses on lifestyle modification and medical management.

Lifestyle modification includes educating patients on the pathogenesis of type 2 diabetes mellitus, dietary changes, the role of exercise, daily management (checking sugar levels), and what are the long-term sequelae of the disease. Enhancing an individuals understanding of type 2 diabetes increases the likelihood of patient compliance. Medical management includes frequent clinic visits, attaining and maintaining recommended goals, and pharmacological intervention. The American Diabetes Association has outlined specific recommended goals for glucose and lipid levels and blood pressure in diabetic patients.

Glycemic control is monitored by the hemoglobin A1c level (HgA1c), pre-prandial and postprandial glucose levels. Physicians check HgA1c levels every three to six months in order to attain and maintain the level to < 7.0%. [1, 2, 3] A HgA1c level of <7.0% reduces the detrimental effects that glycosylated hemoglobin has on the body. Patients record their daily pre-prandial and postprandial glucose levels. The recommendation is to have pre-prandial glucose levels at 90-130 mg/dl and postprandial glucose levels at < 180 mg/dl.[2] Lipid control is monitored by LDL, HDL, and triglyceride levels. The recommended goals are to have LDL < 100 mg/dl, HDL > 40

mg/dl, and triglycerides at <150 mg/dl.[2] Maintaining lipid goals is important because lowering lipids can decrease cardiovascular complications by 20-50%.[1] Blood pressure is also another important factor in the progression of complications from type 2 diabetes mellitus. Good blood pressure control has been found to reduce both microvascular and macrovascular sequelae associated with type 2 diabetes mellitus.[4] The recommended goal for blood pressure for diabetics is <130/80 mmHg.[2]

Attaining and maintaining these recommended goals is vitally important to the management of type 2 diabetes mellitus. Adhering to these recommendations is necessary to deter progression of diabetes and its various complications. Long term effects of type 2 diabetes mellitus include retinopathy, neuropathy, cardiovascular disease (heart disease, stroke, and hypertension), amputations, dental disease, pregnancy complications, hyperosmolar non-ketotic coma, and nephropathy.[1, 2, 5] Physicians, knowledgeable of these complications, focus their diabetic management on prevention. Patients are regularly seen in the clinic to monitor their glucose and lipid levels, their blood pressure, any changes in vision and/or peripheral sensation.

For retinopathy, physicians conduct funduscopic exams, refer diabetic patients to ophthalmology, and then proceed to laser therapy for treatment of eye disease if it develops.[1, 5] Due to the development of neuropathy, patients are instructed to continually check their feet in order to monitor for any skin changes that may result from lack of sensation. Diabetic patients are frequently placed on anti-hypertensive medication in order to maintain a blood pressure < 130/80 mmHg. The anti-hypertensive medications that have been proven to reduce blood pressure and to be renoprotective are ACE

inhibitors and angiotensin II receptor blockers (ARBs). According to the Centers for Disease Control, the risk for developing cardiovascular complications in diabetes mellitus is reduced by 2% with a reduction on systolic blood pressure by 10 mmHg.[1] Therefore, monitoring blood pressure in type 2 diabetes mellitus patients is a mainstay in order to decrease the risk of any cardiovascular complications.

Reduction in blood pressure is important to reduce complications associated with the heart and blood vessels. ACE inhibitors and ARBs are considered renoprotective because they curb the effects that angiotensin II has on blood vessels, allowing for increased blood flow to the kidneys. Developing kidney disease in association with type 2 diabetes mellitus is becoming a leading cause of end stage renal failure in the United States. In 2002, 44% of new cases of renal failure were associated with diabetes mellitus.[1] Diabetic nephropathy is the leading cause of end stage renal disease and has a prevalence of 30-40%.[2, 6]

Diabetic Nephropathy

Diabetic nephropathy is described as the progressive loss of renal function, with decreasing glomerular filtration rate and increasing excretion of albumin.[7] This progressive decline in renal function, and continued elevation of blood pressure, ultimately results in end stage renal disease.[8] Not everyone with type 2 diabetes mellitus will develop nephropathy. Nephropathy is a serious complication and can lead to death; therefore, careful observance of risk factors is important to prevent disease and curb its effects. Risk factors include elevated blood pressure, elevated HgA1c (glycosylated

hemoglobin), cholesterol, smoking, advanced age, lipid levels, obesity, anemia, male gender, race, family history, and high level of insulin resistance.[6,9] The two most important factors that are attributable to development of diabetic nephropathy are blood sugar glucose levels and blood pressure.[7] Therefore, as mentioned previously, attaining glycemic control of HgA1c <7.0% and blood pressure <130/80 mmHg is the mainstay of management of type 2 diabetes and diabetic nephropathy.

Like the risk factors associated with type 2 diabetes mellitus, an important risk factor for diabetic nephropathy is an individuals' race. Diabetic nephropathy affects individuals differently depending on their race and ethnicity. In general, the difference is mainly seen in non-white individuals and white individuals. According to Susztak *et al.*, non-white individuals (namely, Black Americans, Native Americans, and Mexican Americans) are more affected by diabetic nephropathy than White Americans.[10] Non-white individuals with type 2 diabetic mellitus have a higher rate and more rapid progression of nephropathy than white individuals, with non-white individuals developing microalbuminuria at a rate of 4% per year as opposed to white individuals at a rate of 2-3% per year.[7] Nelson *et al.* conducted a study of this occurrence by evaluating the prevalence and incidence of type 2 diabetes in Pima Indians. The Pima Indians were found to have a higher rate of development of proteinuria (>50%) than the rest of the community, despite good control of both blood glucose levels and blood pressure.[7,11] These observations regarding diabetic nephropathy and who it affects are very important to understanding who should be screened for disease.

Screening for diabetic nephropathy is done on all patients with type 2 diabetes mellitus, especially if they have any of the factors that are associated with a higher risk of developing disease. There are three methods of screening for diabetic nephropathy, which include a random albumin-to-creatinine ratio, a 24hour urine collection measuring creatinine clearance, and a timed urine collection.[2, 12] Although the 24 hour urine collection is the gold standard, the random albumin-to-creatinine ratio is the preferred method. It is recommended to screen for microalbuminuria, using an albumin-to-creatinine ratio. This is done annually using a morning urine sample when the individual is in stable glucose control, not acutely ill or has any signs/symptoms of a urinary tract infection.[7] To actually diagnose diabetic nephropathy, an albumin-to-creatinine ratio is checked with multiple samples within a six month window, accounting for day-to-day variations in urinary albumin excretion.[7] Checking for the presence of microalbuminuria occurs over a six month window of time. This is due to transient elevations in albumin-to-creatinine level. These transient elevations occur due to exercise, urinary tract infections, hyperglycemia, febrile illness, severe hypertension, and heart failure.[12, 13] Therefore, the recommendation is to check three times in a six month period, and have at least two positive values before officially diagnosing a patient with diabetic nephropathy.

Although the presence of microalbumin in the urine is used to screen for developing renal disease, it is not specific for diabetic nephropathy. While it is more common for type 2 diabetic patients to develop diabetic nephropathy than any other renal disease, it can occur. Therefore it is important to create a differential diagnosis list and investigate other possible diagnoses in order to correctly determine the cause of the

kidney dysfunction. Diabetic nephropathy may resemble other types of glomerulosclerosis. The differential diagnosis list may include any of the following: IgA nephritis, lupus glomerulosclerosis, membranoproliferative glomerulonephritis, renal amyloidosis, and fibrillar glomerulonephritis.[8] Hypertension can also cause nephropathy on its own apart from diabetes mellitus. The differentiation between hypertensive nephropathy and diabetic nephropathy is made based upon which renal arterioles are affected. In hypertensive nephropathy, there is afferent arteriolization, while in diabetic nephropathy there is both afferent and efferent arteriolization.[8] Differentiation between diabetic nephropathy and any of these other types of glomerulosclerosis is made by analyzing renal tissue with immunofluorescence, electron microscopy, and/or light microscopy.[8]

Biopsy is considered the most accurate and definitive way to diagnose diabetic nephropathy. It is more specific than screening for microalbuminuria because it shows the specific histologic changes present in diabetic nephropathy. The histological diagnosis is "diffuse and nodular glomerulosclerosis, tubulointerstitial fibrosis and atrophy, and with degrees of hyaline arteriosclerosis and arterial sclerosis".[8] Mesangial expansion is the earliest change that occurs in renal disease that is due to type 2 diabetes mellitus.[8] Other characteristic histologic changes that occur in diabetic nephropathy are glomerulosclerosis (diffuse and nodular), hyaline arteriolization (afferent and efferent), IgG and albumin deposition on the basement membrane, and podocyte reduction.[7, 8] There is a progression from diffuse glomerulosclerosis to nodular glomerulosclerosis that occurs in diabetic nephropathy. Initially there is thickening of the basement membrane

with mesangial matrix accumulation, which leads to the development of Kimmelsteil-Wilson nodules.[8] Kimmelsteil-Wilson nodules are specific for diabetic nephropathy, but they are not pathognomic.[8] It is the association of all of these histologic changes that allow for a more precise diagnosis of diabetic nephropathy based on biopsy.

Although biopsy is more specific, the diagnosis of diabetic nephropathy is more commonly determined by clinical and laboratory findings. The least invasive method of determining a diagnosis is the standard because it has the least risk of developing a complication. As mentioned previously, screening for and diagnosing diabetic nephropathy is clinically done using the urinary albumin-to-creatinine ratio. Microalbuminuria is defined as the detection of an increased amount of albumin in the urine, but it cannot be detected by the urine dipstick method.[14] It is defined as 30-299 mg/dl and referred to as "incipient nephropathy".[2] Checking the albumin-to-creatinine level initially occurs at the time of diagnosis of type 2 diabetes mellitus because typically the diagnosis of type 2 diabetes mellitus occurs late and the development of renal damage has already started.[12] Clinically, the detection of microalbuminuria is the earliest finding of diabetic nephropathy; therefore it is used as a screening tool.

Diabetic nephropathy progresses over time from minimal damage to the kidney to more pronounced damage. According to Remuzzi *et al.*, the progression of diabetic nephropathy occurs in five stages.[9] In the first stage, the glomerular filtration rate is increased. The second stage is considered the 'clinically silent stage' where there is hyperfiltration and hypertrophy. The third stage is 'initial nephropathy'. It consists of microalbuminuria, increased blood pressure, and decreased glomerular filtration rate.

The fourth stage is considered 'overt nephropathy' where there is macroalbuminuria, a greater increase in blood pressure, and more of a decline in glomerular filtration rate. The final stage results in the individual finally having to undergo renal replacement therapy, specifically dialysis.[9]

Microalbuminuria is initially used as a screening tool, but it has become a marker for prediction of mortality and cardiovascular death. It is not used as a predictor of progression of renal disease because there is not a strong correlation between higher levels of microalbuminuria and worsening renal disease.[14] Otu *et al.* found that microalbuminuria was not a good predictor of underlying glomerular damage, but was a good predictor of cardiovascular disease.[15] It is a marker for generalized endothelial damage; therefore it is a good marker for microvascular and marcrovascular disease, including cardiovascular death.[7, 14] Therefore, physicians should use the urinary albumin-to-creatinine ratio to gauge the patients' risk of progression of cardiovascular disease.

Microalbuminuria indicates damage to the renal vascular system caused by elevated glucose and elevated blood pressure. Glycosylated hemoglobin and angiotensin II have detrimental effects on the renal arterioles, leading to protein in the urine. Initially, the proteins that leak through the arterioles are in small amounts but as the disease progresses the proteins become bigger and in greater amount. Identifying those with microalbuminuria is important in order to halt the progression of renal disease to overt nephropathy. According to Bruno *et al.*, individuals with microalbuminuria are more likely than individuals with normoalbuminuria (< 30mg/dl) to develop diabetic nephropathy, with a 42 % increased risk of progression of the disease.[16] Therefore, those

who are leaking small amounts of protein will not definitely go on to develop more advanced disease, but some do.

Overt nephropathy is the term that refers to the presence of macroalbuminuria. Macroalbuminuria refers the progression of the disease to larger amounts of protein passing through the glomerulus into the urine and is detectable by urine dipstick. It is defined as the urinary albumin-to-creatinine level $\geq$ 300 mg/dl.[2] Not everyone with microalbuminuria will progress to overt nephropathy. The risk factors that are associated with developing macroalbuminuria are HDL, apoproteinB, fibrinogen, HbA1c.[16] According to Bruno *et al.*, only about 3.7% of diabetes mellitus patients proceed to develop overt nephropathy; 2.6% initially had normoalbuminuria and 5.4% had microalbuminuria.[16] The occurrence of macroalbuminuria comes with an increased risk of renal failure. The glomerular filtration rate continually declines at a rate of 10-12 ml/min/year once albumin-to-creatinine is detected in the urine.[9, 16] This further reduction in the glomerular filtration rate, without any intervention, will ultimately result in necessitating renal replacement therapy.

As a result of the severity of renal failure associated with developing macroalbuminuria, physicians need to regularly monitor urinary albumin-to-creatinine levels with frequent laboratory tests and management through medication. Keeping albumin-to-creatinine levels < 30mg/dl (normoalbuminuria) will further reduce the risk of developing diabetic nephropathy and subsequently renal failure. Regardless of this reality, many physicians do not regularly check for microalbuminuria. According to Lane *et al.*, the inconsistent use of the microalbumin assay is the result of lack of

availability of the test, confusion with the units, the increased turn-around time, and/or the belief of many clinicians that checking is not needed since patients are already placed on renoprotective medications.[14] The latter thought is incorrect. As previously stated, microalbuminuria is not an indicator of progression of renal disease; instead, it is a predictor for cardiovascular death. Regularly checking the urinary albumin-to-creatinine level, even when patients are on anti-hypertensive medication, permits the clinician the ability to titrate the medication based on the level of microalbuminuria present.[14] Titrating provides a more enhanced level of renoprotection and prevention of the progression of cardiovascular disease associated with type 2 diabetes mellitus.

Using anti-hypertension medication is one method in the management of preventing and treating diabetic nephropathy. Once microalbuminuria is present, physicians need to start their patients on anti-hypertensive medication in order to provide renoprotection from angiotensin II. Angiotensin II causes efferent glomerular arteriole constriction.[7,8] This occurs by stimulating glycation of end product formation, mesangial cell proliferation, and accumulation of mesangial matrix.[7,8] The effects of angiotensin II causes increased permeability of the glomerular arteriole to protein, ultimately leading to diabetic nephropathy. Preventing the action of angiotensin II will preserve the filtering quality of the glomerulus, decrease the amount of protein that is excreted, and decrease intraglomerular pressure.[7,8] According to the UKPDS study the lower the blood pressure, the lower the risk of microalbuminuria.[4] Therefore, one of the uses of anti-hypertensive medication in type 2 diabetes mellitus is to prevent the development of renal disease.

Preventing diabetic nephropathy is also accomplished with glycemic control. Hyperglycemia has a profound effect on renal function. Elevated blood glucose levels create a defect in the mitochondrial transport system, resulting in increased reactive oxygen species.[8] The increased oxidative stress creates glycation and formation of cytokines and growth factors.[8] These mediators increase the production and deposition of extracellular matrix resulting in glomerulosclerosis and tubulointerstitial fibrosis.[7, 8] Maintaining good glycemic control to HbA1c < 7.0% will reduce the effects that hyperglycemia has on the kidney. In the UKPDS study, the lower the blood sugar glucose level was, the lower the risk of developing microalbuminuria.[3] Achieving glycemic control is accomplished with lifestyle modifications, diet and exercise, and through pharmacologic means.

Management of type 2 diabetes mellitus and microalbuminuria also involves reducing the cardiovascular risk associated with developing diabetic nephropathy. Maintaining blood pressure to < 130/80 mmHg will reduce the progression of renal disease.[9] Various studies have reviewed which types of anti-hypertensive medication that are the most renoprotective. The UKPDS study showed that ACE inhibitors and β blockers reduced the risk of death and complications due to diabetes mellitus.[4] The RENAAL study demonstrated that ARBs, specifically Losartan, decreased the urinary protein level by 35% and reduced the risk for end point measures (plasma creatinine, end stage renal disease, or death) by 22%.[9, 17] In the IDNT study, it was found that ARBs, specifically Irbesartan, lowered the risk of end points by 20%.[9, 18] Other studies have reviewed the use of combination of anti-hypertensive medication. In the TRAVEND

study, the use of verapamil and trandolapril proved to have better metabolic control than enalapril and hydrochlorothiazide.[9, 19] In the BENEDICT study, the use of VeraTran (verapamil + trandolapril) reduced proteinuria and slowed GFR decline more than trandolapril alone.[9, 20] The study also showed that trandolapril alone delayed the onset of microalbuminuria by a factor of 2.1 and decreased the risk for microalbuminuria by 53% as compared to verapamil alone, which showed no significant effects.[20] As a result of reviewing these studies, using any anti-hypertensive medication for blood pressure control is better than not using anything. But, the studies have shown that some anti-hypertensive medications are better than others at reducing the development and progression of renal dysfunction. ACE inhibitors and/or ARBs are the preferred anti-hypertensive medication as compared to calcium channel blockers, diuretics, and β blockers. There have been no head to head studies between ACE inhibitors and ARBs.

Overall, the management of diabetic nephropathy is complicated. It consists of prevention, through the use of lifestyle changes and medication, and treatment of the disease. Treatment of diabetic nephropathy includes the use of anti-hypertensive medication, namely ACE inhibitors and ARBs, protein restriction to ≤0.8 g/kg/body weight/day, monitoring of serum potassium, achieving glycemic control and blood pressure control, and referring to a nephrologist if glomerular filtration rate significantly decreases.[2] Involving nephrology early is important in management because having a treatment plan of starting dialysis is better for the patient than emergently starting renal replacement therapy.[7]

Research is currently being done to continue studying type 2 diabetes mellitus, diabetic nephropathy, and the complications associated with both. Namely, research is being conducted to identify better screening measures. Since microalbuminuria is not specific for diabetic nephropathy nor is it an indicator of disease progression, researchers want to identify a screening tool that specifically identifies those who are at risk of developing diabetic nephropathy. Proteomic profiling is a fast growing area of research. It identifies urinary proteins that are associated with diabetic nephropathy before any clinically identifiable changes in renal function occur, namely microalbuminuria.[15] Otu *et al.* have discovered a urine protein signature that was able to accurately distinguish between individuals who did and did not develop diabetic nephropathy over a ten year period.[15] Susztak *et al.*, also uncovered polypeptides whose pattern was consistent with diabetic renal damage.[10] Proteomic profiling would provide for earlier detection of diabetic nephropathy than the current screening for microalbuminuria.

There are other studies that are focused on identifying newer screening measures for the development of diabetic nephropathy. Some of these studies focus on elucidating the relationship between visceral disease and somatic structures. By uncovering this relationship, researchers and clinicians hope to reveal the importance of palpatory findings associated with type 2 diabetes mellitus and/or diabetic nephropathy. Licciardone *et al.* studied which palpatory findings, if any, were associated with type 2 diabetes mellitus. It was identified that when palpating the spine and paraspinal musculature, immobility of segmental vertebral motion and tissue changes were most commonly associated with individuals who had type 2 diabetes mellitus.[21] Specifically,

the most common associated finding was tissue change found at the level of T_{11}-L_2.[21] According to the study, tissue changes consisted of doughy, ropy, thickened, or fibrotic interstitial tissue.[21] The conclusion is that there is an association between visceral disease found in patients with type 2 diabetes mellitus and somatic structures that result in these palpatory changes.

Viscerosomatic Reflex

The underlying mechanism that connects visceral disease with somatic structures is a viscerosomatic reflex. A viscerosomatic reflex is defined as the effect that afferent stimuli from visceral disease has on somatic tissues.[22] Much research has been done regarding this subject to determine physiologically whether a proposed mechanism exists and, if so, how and why. It was concluded that a stimulus from visceral organs is able to affect somatic structures due to the phenomena of convergence and facilitation.

Convergence refers to the process of visceral, cutaneous, and somatic pathways converging together at the dorsal horn permitting the relaying of information from one pathway to another. A viscerosomatic reflex begins with afferent nociceptive impulses from visceral receptors. The neural signals are transmitted by Aδ and C fibers.[23] Aδ fibers are small peripheral myelinated neurons and C fibers are peripheral unmyelinated neurons.[24] These fibers enter the dorsal root ganglia and project branches to somatic efferents and visceral efferent. They contribute to transmission of information that results in the experience of pain.[24] These nociceptive impulses enter the spinal cord at the dorsal horn and synapse with interconnecting neurons.[22, 23] They then stimulate the

sympathetic and peripheral motor efferents, resulting in sensory and motor changes in the somatic tissues, viscera, blood vessels, and skin.[22, 23, 25] In the dorsal horn, the convergence of information from various pathways stimulates the neurons in three different systems. The spinoreticular, spinothalamic, and spinomesencephalic systems, which respond to both somatic and visceral stimuli, are all activated with convergent information.[26] According to van Buskirk, somatosomatic, somatovisceral, viscerosomatic, and viscerovisceral reflexes result from nociceptive stimuli that have converged at the dorsal horn.[24] Once convergence occurs, there is now a connection between the viscera and the soma allowing for changes in the viscera to affect the soma, and vice versa.

The impulses created by the visceral afferent nerves to the spinal cord create widespread motor activity in the soma and viscera.[27] For example, Qin *et al.* studied convergence by looking at the role of the interconnecting neurons. Thoracic respiratory interneurons (TRINs) participate in intraspinal processing of information from the soma and the visceral. TRINs demonstrated that they received both noxious and non-noxious inputs from both somatic and visceral structures.[28] Viscerosomatic and viscerovisceral convergence patterns were demonstrated when TRINs were activated.[28] This example of TRINs proves that within the dorsal horn, where interconnecting neurons like thoracic respiratory interneurons live, convergence exists and links visceral and somatic activity.

Convergence is most frequently considered as the cause of 'referred pain'. According to Ammons *et al.*, the pain of renal disease is associated with circuits that relay renal and somatic input.[25, 29] Hancock used the term "postactivation depression" to

refer to the desensitization of neurons at receptor sites when convergence occurs.[30] This results in a depolarization of the cutaneous afferent neurons causing somatic structures to be more susceptible to stimuli.[30] 'Postactivation depression' has also been referred to as facilitation.

Facilitation describes the phenomena of nociceptors that are held at lower than normal threshold level. Once nociceptors converge in the dorsal horn, they release chemicals (neurotransmitters). The chemicals decrease the threshold of activation of the nociceptors, resulting in neurons that respond to lower than normal stimuli.[23, 24] The chemicals create a positive feedback loop that is reinforced whenever there is a stimulus.[23, 24] These nociceptor reflexes continue to relay information using the spinal cord connections.[24] Many times this process occurs without the perception of pain. As a result, weaker visceral afferent stimuli can affect a somatic response when facilitation has previously occurred.[22]

Somatic Dysfunction and Palpatory Changes

The connection between the visceral and somatic structures results in physiologic changes in the soma. This is an example of somatic dysfunction. Somatic dysfunction is defined as "impaired or altered function of related components of the somatic system, including skeletal, arthrodial, and myofascial structures and related vascular, lymphatic, and neural elements".[23] The incidence of somatic dysfunction varies throughout the spine. It is most predominant in the transition areas of the spine, namely the upper thoracic and lumbosacral regions.[31] There are various factors that affect the presence of

somatic dysfunction. Some include posture, short leg, handedness, and visceral reflexes.[22] Somatic dysfunction may indicate the details of disease. Specifically, it can demonstrate how the disease is progressing, its location, and its severity.[32] Differentiating between visceral and somatic disease is dependent on the palpatory changes that occur with a viscersomatic reflex.

Viscerosomatic reflexes manifest themselves in somatic tissue in a variety of ways. According to Beal, these somatic changes include hyperesthesia, vasomotor pilomotor and sudomotor phenomena, rigidity of the musculature, localized muscle contraction with spasm, and paravertebral muscle splinting.[22] Eble *et al.* demonstrated the relationship between palpatory somatic changes and visceral stimulation. A paravertebral muscle contraction occurred when the renal pelvis, ureters, fallopian tube, small intestine and colon in rabbits were stimulated.[22, 33] This provides evidence that the relationship between specific organs can cause a specific palpable somatic dysfunction when the visceral afferents are stimulated.

There are multiple types of palpatory findings associated with somatic dysfunction. Primarily they can be differentiated based upon whether the injury and reaction are acute or chronic. Acute dysfunction manifests itself in somatic tissues in a variety of ways. Acute somatic dysfunction can include doughy boggy texture of the tissue, hyperesthesia, increase in skin temperature, increase in moisture, increase in skin drag, an increase in subcutaneous fluid, diffuse muscle contraction, and thickening of the skins texture.[22, 32] Once the acute phase of somatic dysfunction subsides, the tissues either heal or become chronic.[22] Chronic somatic dysfunction manifests as more

pronounced thickening of the skin and subcutaneous tissue, localized muscle contraction which become hard and tense, deep muscle splinting and contraction, abnormal hardness and rigidity, absence of hypesthesia, and decrease in motion.[22, 32]

These skin and tissue changes are important because they become palpably evident and may indicate the presence of underlying visceral disease. A subclinical disease may manifest its somatic dysfunction as muscle irritability, hypertonicity, subcutaneous edema.[22] Osteopathic physicians are able to identify a viscerosomatic reflex through their understanding of the relationship between the viscera and soma and through their ability to palpate these changes.

Diagnosing a viscerosomatic reflex through palpation necessitates the clinician to fully understand what the reflex is, how it works, and how it manifests itself in somatic tissue. Criteria for diagnosing a viscerosomatic reflex include two or more adjacent spinal segments with somatic dysfunction, deep muscle splinting, resistance to segmental joint motion, and/or skin and subcutaneous changes consistent with the acuity or chronicity of the reflex.[22, 34] The clinical suspicion for a viscerosomatic reflex increases when the somatic change is continually resistant to manipulative treatment.[22] Somatic dysfunction can also detect the duration of the visceral disease. The greater the number of spinal segments involved, the higher likelihood that the somatic dysfunction is visceral in nature.[22] Although visceral disease may manifest itself as somatic dysfunction, it is not the only cause. The diagnosis must also take into account whether there is a history of associated visceral disease and correlate that with the findings of somatic dysfunction.[22]

Identifying these somatic changes involves a palpatory exam where the physician places their hands on patients and physically senses what the underlying tissues feel like. To create some uniformity, Beal has described in detail how the palpatory exam should be conducted. Clinicians first place their fingers on the skin surface and ascertain its quality.[22] Next, they will apply a compressive force to determine the consistency and viscoelastic quality of the tissue.[22] Lastly, the clinician will conduct the compression springing motion test, by contacting the transverse processes bilaterally and springing anteriorly to assess the quality of motion.[22] This exam may be conducted with the patient seated, supine, standing, or prone. Through this palpation, the physician will be able to ascertain the TART changes associated with viscerosomatic reflexes.

TART is an acronym for tissue texture changes, asymmetry, restriction of motion, and tenderness.[35] Many physicians use this acronym in their clinical physical exam to identify areas of a patients' body that indicates the presence of somatic dysfunction. Tissue texture changes include temperature of the skin, dryness, dough, ropy, thickened or fibrotic tissue, tone of the tissue.[21, 35] Asymmetry refers to the presence of any misalignment, masses, or crepitus.[35] Restriction of motion is defined as immobility of segmental vertebral motion or of gross active and/or passive motion of the body.[21] Tenderness refers to pain elicited.

Using TART changes is also important in assessing for the presence of somatic dysfunction related to viscerosomatic changes. Although the other aspect of TART are always evaluated and recorded, tissue texture changes has been found to be the most significant marker for identifying viscerosomatic reflexes.[22] Range of motion, namely

restriction of motion, was found to have the least association with viscerosomatic reflexes.[22] According to Denslow, the importance of assessing for somatic dysfunction/TART changes is that tissue texture can represent improvement or regression of a disease state.[32]

Somatic Dysfunction and Cardiovascular Disease

The somatic dysfunction created from the connection between the visceral and somatic tissues is related to the sympathetic nervous system innervation. Referral pain to somatic structures from visceral disease is located in the same spinal innervation region as the diseased organ.[36] For example, the heart is innervated by the sympathetic nervous system at the thoracic level 1 to the thoracic level 5 or 6 (T_1-$T_{5/6}$).[34, 23] If the heart is diseased, it will send an afferent nociceptor stimulus to the dorsal horn of the spinal cord, where convergence will then send efferent information to the somatic tissue. The somatic tissue that is affected and that will subsequently exhibit somatic dysfunction, will be located in the region of T_1-$T_{5/6}$. Therefore palpatory changes that occur as a result of a viscerosomatic reflex occur in the same sympathetic innervation region as the diseased organ.

To further elucidate this example of heart disease and somatic dysfunction located in the region of T_1-$T_{5/6}$, we look at studies conducted by Beal *et al.* and Gwirtz *et al.* Beal *et al.* conducted a research study to identify whether there was a correlation between palpatory changes and cardiovascular disease. Palpatory changes of somatic dysfunction were measured as tissue changes, asymmetry of the transverse processes or ribs, and

mobility of the spine and ribs.[34] It was concluded that there was a correlation between cardiovascular disease and vertebral segments T_{1-5}.[22, 34]

Subsequent studies researched this association in more detail. Beal *et al.* further examined the relationship between somatic dysfunction and cardiovascular disease to determine if the palpatory changes were a predictor of cardiovascular disease, as confirmed with cardiac catherization.[37] The correlation between the presence or absence of somatic dysfunction and cardiovascular disease was found to be 79%.[37] Although there is a strong correlation between palpatory change and disease, Beal *et al.* states that it is not realistic to use palpation as a screening tool in asymptomatic individuals. The prevalence of coronary artery disease and somatic dysfunction in asymptomatic subjects was found to be 4%.[22, 37] Beal *et al.* does recommend using palpation to screen individuals who have high risk factors for disease.[37]

Gwirtz *et al.* studied the viscerosomatic reflexes associated with myocardial infarction in dogs and confirmed these changes using EMG.[23] The palpatory changes were most notable at T_{2-5} in the paraspinal musculature.[23] Once the somatic dysfunction was identified, it was confirmed using EMG. The EMG activity within the region of T_{2-5} confirmed the connection between the induced myocardial infarction and the somatic tissue. The EMG showed that there were tissue changes and increased muscle tone in the thoracic spine at T_{2-5} which represents the presence of a viscerosomatic reflex.[23]

Somatic Dysfunction and Renal Disease

The viscerosomatic relationship between cardiac activity and somatic tissues has been thoroughly studied and palpatory response to cardiac visceral disease has been adequately documented. In 1975, Nicholas observed that there was a correlation between genitourinary system disease and somatic dysfunction located at the lower thoracic and lumbar areas.[38] It was found that the majority of somatic dysfunction was at the second lumbar segment (L_2) with 67.4% of patients with this specific palpatory finding.[38] Despite this recorded correlation between the genitourinary system and somatic dysfunction, there has not been much research in the field of viscerosomatic reflex of renal origin. Therefore it can be theorized that based on renal anatomy and physiology, a renal viscerosomatic reflex will manifest itself as somatic dysfunction just as the cardiac viscerosomatic reflex created palpatory changes.

Neural renal anatomy consists of two renal receptors that will ultimately stimulate renal visceral afferent fibers. These two renal receptors are mechanoreceptors and chemoreceptors.[25, 29] Renal mechanoreceptors are activated by renal vein occlusion, ureteral occlusion, and increased renal perfusion pressure.[29] Renal chemoreceptors are activated by renal ischemia.[29] Once the renal mechanoreceptors and chemoreceptors are activated, they send impulses via visceral afferent fibers. As described earlier, the renal afferent fibers enter the spinal cord through the dorsal horn at the spinal level associated with renal sympathetic nervous innervation. The sympathetic innervation to the kidney is at the thoracolumbar region, $T_{10/11}$-L_2.[22, 25, 29] The stimulated renal afferent nerves, which

include Aδ and C fibers, enter the spinal cord at the lower thoracic and upper lumbar region, converge with other pathways and emerge at the somatic level of $T_{10/11}$-L_2.[22, 25, 39]

Johnston *et al.* studied the association between renal disease and somatic dysfunction. It was concluded that there was a higher incidence of palpatory findings associated in the region of $T_{9\text{-}12}$ in individuals with renal failure.[22, 39] An increase in skin temperature was the palpatory finding with the most significance.[22, 39] Johnston *et al.* found that in the region of $T_{9\text{-}12}$, there was an increase in blood flow and heat transfer as determined by thermographic imaging.[39] This finding aids in the palpatory analysis that there was an increase in skin temperature at the spinal level of $T_{9\text{-}12}$.

Understanding renal anatomy and physiology is essential to identifying the presence of and understanding the significance of the relationship between renal viscerosomatic reflexes and somatic dysfunction. The sympathetic innervation to the kidney has been ascribed from anywhere between T_9-L_2. Most research most *specifically* identifies T_{10}-L_2 as the sympathetic innervation to the renal system. Based upon previous research and anecdotal evidence, the relationship between visceral organs and somatic tissue manifests itself as somatic dysfunction (TART changes). These TART changes can be identified through palpation. Therefore, physicians can identify visceral disease by using their hands to palpate the spine and paraspinal musculature that corresponds to the sympathetic innervation of that diseased organ.

Hypothesis

The purpose of this study was to evaluate the efficacy of osteopathic palpatory findings in screening for diabetic nephropathy (renal disease) in individuals known to have type 2 diabetes mellitus. There are two aims that guided this study.

Specific Aim 1: To assess whether osteopathic palpatory findings will be more associated with type 2 diabetics than non-diabetic people.

Hypothesis 1: *Osteopathic palpatory findings at the thoracolumbar level of T_{10}-L_2 will be more prevalent in subjects with type 2 diabetes mellitus than in subjects without disease.* This was assessed by comparing recorded palpatory findings of the control and disease group. The palpatory findings included TART changes.

Specific Aim 2: To assess whether osteopathic palpatory findings will be associated with diabetic nephropathy.

Hypothesis 2: *Osteopathic palpatory findings at the thoracolumbar level of T_{10}-L_2 will be associated with type 2 diabetes mellitus and the development of renal disease.* This was assessed by comparing recorded palpatory findings of the disease group, for renal and non-renal disease subjects. The palpatory findings included TART changes.

CHAPTER II

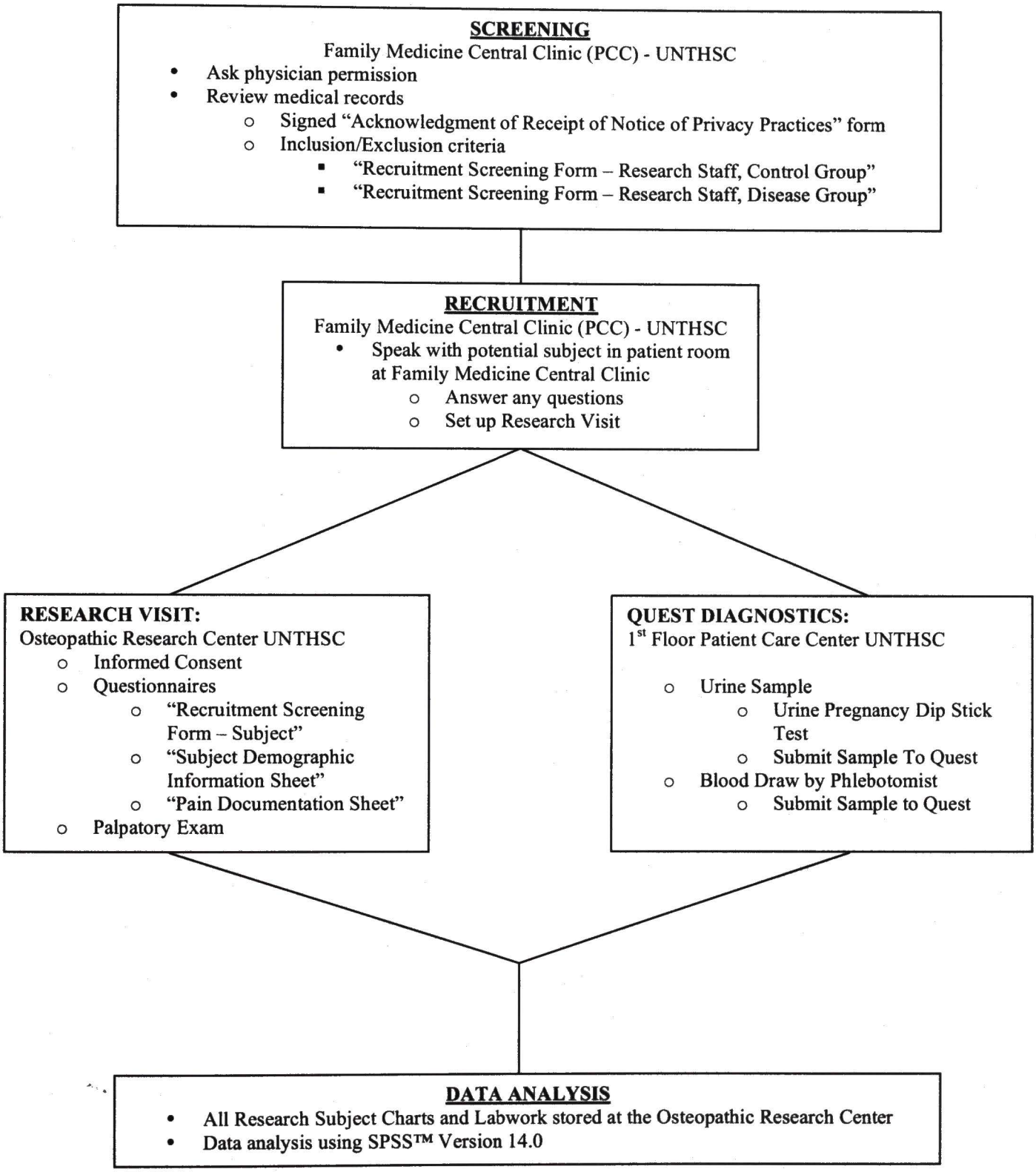
RESEARCH DESIGN AND METHODS

This study was approved by the Institutional Review Board at the University of North Texas Health Science Center. All subjects were screened and recruited from the Family Medicine Central Clinic located in the Patient Care Center on the University of North Texas Health Science Center campus.

Participants

All subjects met inclusion and exclusion criteria and signed informed consent prior to participating in the study. A total of 30 subjects were screened, recruited, and participated in the study. Ultimately only 26 subjects were included and their data analyzed. Although all thirty subjects met inclusion and exclusion criteria, laboratory data for four subjects were missing. Therefore, these four subjects were excluded from data analysis. Based upon their past medical history and laboratory findings, the subjects were placed in two groups: the control group (n=10) and the disease (type 2 diabetes mellitus) group (n=16). The disease group was further subdivided into two groups: the renal disease group (n=10) and the no renal disease group (n=6).

Figure 1: Research Design Flowchart



Screening and Recruitment

Screening and recruitment by the research staff occurred at the Family Medicine Central Clinic. The research staff consisted of an osteopathic manipulative medicine predoctoral fellow. The osteopathic predoctoral fellow is a 3rd or 4th year medical student at the Texas College of Osteopathic Medicine who is spending an extra year learning, practicing, and teaching osteopathic manipulative medicine.

The research staff went to the Family Medicine Central Clinic once or twice a week to screen for potential subjects. First the research staff asked the physician if any scheduled patients would qualify for the study. Then the research staff reviewed the chart of any potential subjects. While reviewing the medical record, the research staff ensured that each patient's medical record contained a signed "Acknowledgment of Receipt of Notice of Privacy Practice" form, which indicates that the patient has received and read the "Notice of Privacy Practices" form.

As standard practice, every patient at the Family Medicine Central Clinic receives and read the "Notice of Privacy Practices" form. This form describes how the patients' medical information is used and disclosed, and how they are able to access their own medical information. Item 16 of the "Notice of Privacy Practices" form addresses the use of the medical record for research purposes, stating that the patients' medical information may be used and disclosed for research purposes. After reading through the "Notice of Privacy Practices" form, each patient is given the "Acknowledgment of Receipt of Notice of Privacy Practices" form and signs it acknowledging that they have received and accepted the terms of the privacy practices form. After signing the "Acknowledgment of

Receipt of Notice of Privacy Practices" form, this form is placed permanently in the medical record. The research staff recorded on the "Recruitment Screening Form – Research Staff" that the medical record contains a signed "Acknowledgment of Receipt of Notice of Privacy Practices" form.

After the research staff verified that the "Acknowledgment of Receipt of Notice of Privacy Practices" form was signed and located within the chart, they then reviewed the rest of the medical record to screen each potential subject and determine if they qualified for the study based upon inclusion and exclusion criteria. The inclusion and exclusion criteria varied based upon to which group they belonged.

The inclusion criteria for the control group consisted of the following:

- Subjects were 18 years of age or older, male or female. Children were not included in this study because the development of diabetic nephropathy occurs at a lower rate in children than in adults.
- Subjects had no clinical diagnosis of type 2 diabetes mellitus as determined by the subjects' medical record from the Family Medicine Central Clinic at the Patient Care Center.
- Subjects did not have a clinical diagnosis of renal disease as determined by the subjects' medical record from the Family Medicine Central Clinic at the Patient Care Center.

The inclusion criteria for the disease group consisted of the following:

1. For the subgroup with no history of diabetic nephropathy:

- Subjects were 18 years of age or older, male or female. Children were not included in this study because the development of diabetic nephropathy occurs at a lower rate in children than in adults.
- Subjects had a known clinical diagnosis of type 2 diabetes mellitus as determined by the subjects' medical record from the Family Medicine Central Clinic at the Patient Care Center.
- Subjects did not have a clinical diagnosis of renal disease as determined by the subjects' medical record from the Family Medicine Central Clinic at the Patient Care Center. Urinary microalbumin/creatinine level < 30 mg/dl.

2. For the subgroup with a history of diabetic nephropathy:
    - Subjects were 18 years of age or older, male or female. Children were not included in this study because the development of diabetic nephropathy occurs at a lower rate in children than in adults.
    - Subjects had a known clinical diagnosis of type 2 diabetes mellitus as determined by the subjects' medical record from the Family Medicine Central Clinic at the Patient Care Center.
    - Subjects did not have a clinical diagnosis of renal disease as determined by the subjects' medical record from the Family

Medicine Central Clinic at the Patient Care Center. Urinary microalbumin/creatinine level $\geq$ 30 mg/dl.

The exclusion criteria for this study (for control and disease groups) consisted of the following:

- Type 1 diabetes mellitus
- Pregnancy (current pregnancy or recent pregnancy – assessed by self report and by urine pregnancy test). Pregnancy will be excluded due to possible development of gestational diabetes.
- History of non-diabetic renal disorders (such as acute tubular necrosis, polycystic kidney disease, acute renal failure, non-diabetic renal disease)
- Acute genitourinary disease (including but not limited to urinary tract infection and nephrolithiasis)
- Chronic medical disease affecting the adrenals, large intestine, appendix, urinary bladder, ureters, prostate, and uterus as these organs also have the same sympathetic innervation as the kidney, located at T_{10}-L_2.

The research staff specifically looked at the medical record for the potential subjects' age, diagnosis of type 2 diabetes mellitus, past medical history of Crohn's Disease, Conn's Disease, Cushing's Disease, Prostatitis, Benign Prostatic Hypertrophy, Ulcerative Colitis, Addison's disesase, Irritable Bowel Syndrome, and/or Pelvic Inflammatory Disease. Having a past medical history that includes any of the above mentioned medical conditions is an exclusionary criterion because the innervation region related to these diseases is the same innervation region related to diabetic nephropathy.

There is no increased risk related to individuals with any of these diseases for this research study. However, the inclusion of individuals with these diseases would distort the results, making it difficult to attribute the palpatory findings to diabetic nephropathy. The research staff also reviewed the medical record for a urinary microalbumin/creatinine level and a plasma glucose level from the past year, based upon whether they were in the control group of the disease group.

The control group consisted of subjects that had no history of type 2 diabetes mellitus and no history of renal disease. Therefore, the research staff reviewed the medical record to ensure that the potential subject did not have a previous diagnosis of type 2 diabetes mellitus and no previous diagnosis of renal disease, all in accordance to the inclusion and exclusion criteria. The research staff also checked the medical record for a most recent documented plasma glucose level. The potential subjects' last plasma glucose level must be < 126mg/dl to qualify them for the control group. The research staff documented on the "Recruitment Screening form – Research Staff, Control Group" the necessary information regarding inclusion and exclusion criteria and the last plasma glucose level for all potential control group subjects.

The disease group consisted of subjects that have a known diagnosis of type 2 diabetes mellitus. Therefore, the research staff reviewed the medical record to ensure that the potential subject has a diagnosis of type 2 diabetes mellitus. Furthermore, the disease group was subdivided into those with a diagnosis of diabetic nephropathy and those without a diagnosis of diabetic nephropathy. Therefore, the research staff reviewed the medical record to determine if the potential subject has or does not have a

diagnosis of diabetic nephropathy. The research staff also checked the medical record for their last urinary microalbumin/creatinine level. A urinary microalbumin/creatinine level of < 30 mg/dl indicates that the potential subject does not have renal disease; a urinary microalbumin/creatinine level ≥ 30 mg/dl indicates that the potential subject does have renal disease. The research staff documented on the "Recruitment Screening Form – Research Staff, Disease Group" the necessary information regarding inclusion and exclusion criteria and last urinary microalbumin/creatinine level for all potential disease group subjects.

Not every patient had a documented plasma glucose level or a urinary microalbumin level from the past year. Therefore, final division of the subjects into control and disease groups, and subgroups renal and no renal disease was officially made after the study was completed and labwork from the study was reviewed. The determining factor for the division of control and disease group was that the control group subject did not have type 2 diabetes mellitus and had a plasma glucose level < 126 mg/dl. The determining factor for the division of the disease group into renal disease and no renal disease was a previous diagnosis of diabetic nephropathy and/or laboratory findings indicative of renal disease. These laboratory findings included: urinary microalbumin/creatinine ratio ≥ 30 mg/dl, BUN > 20 mg/dl, plasma creatinine > 1.2 mg/dl, urinary creatinine > 320 mg/dl, BUN/creatinine ratio > 22, and eGFR ≥ 60 ml/min/1.73 m^2. If any of these laboratory values was elevated, they were considered to be in the renal disease group.

After the research staff reviewed the potential subejcts' medical record and determined their eligibility for the study, the research staff spoke with the potential subjects to recruit them to the study. The research staff spoke to the potential subject on the day of their Family Medicine Central Clinic visit, in the patient exam room. During this encounter, the research staff explained the research study in its entirety, determined their interest in participating, and answered any initial questions they had. If the potential subject was interested in the research study, they went to the Osteopathic Research Center to participate.

Data Collection

The data was collected between March 2007 and November 2007 at the Osteopathic Research Center and at Quest Diagnostics laboratory on the University of North Texas Health Science Center campus. It consisted of the research visit and the laboratory visit, both occurring the same day.

The research visit would take place at the Osteopathic Research Center on the campus of the University of North Texas Health Science Center. This was one visit which lasted about an hour. During this time, informed consent, questionnaires, and the palpatory exam took place.

After the research staff answered any questions the potential subject had and if the potential subject wanted to continue to participate in the study, the potential subject signed the informed consent document. The signed informed consent document verifies the subjects' understanding of the study for which they volunteered. The subjects filled

out questionnaires regarding past medical history and demographic information, including age, gender, and race/ethnicity. These questionnaires are called "Recruitment Screening Form – Subject" and "Subject Demographic Information Sheet".

Afterwards, the diagnostic staff took the subjects vitals and conducted the palpatory exam. The diagnostic staff included two osteopathic predoctoral fellows. These osteopathic predoctoral fellows did not participate as a member of the research staff and they were blinded as to the diabetic status and/or diabetic nephropathy status of each individual subject. Two osteopathic predoctoral fellows participated as diagnostic staff. Each took turns conducting the palpatory exam.

The diagnostic staff took the subjects vital signs, which included respiratory rate and pulse. They also recorded the subjects' initial pain level, and documented it on a form entitled "Pain Documentation Sheet". This form was a pain scale that ranged from 0-10, where 0 was no pain and 10 was most/worst pain they had ever had. Once vitals were obtained and the pain questionnaire was completed, the diagnostic staff conducted the palpatory exam on the subjects. The members of the diagnostic staff were trained by me, the Co-investigator, to perform the palpatory exam according to the protocol.

During the exam, the diagnostic staff assessed for specific osteopathic palpatory findings and recorded their findings on a form entitled "Palpatory Exam Documentation Sheet". Specifically, they assessed for TART changes. TART is an acronym that stands for Tissue texture changes, Asymmetry, Restriction of motion, and Tenderness.

The "Palpatory Exam Documentation Sheet" was a three page form filled out by the diagnostic staff. The diagnostic staff recorded their palpatory TART findings on this

form. The form was divided into four main sections: **T** – Tissue texture changes, **A** – Asymmetry, **R** – Restriction of Motion, and **T** – Tenderness.

The **T** section was divided into two groups: Acute Red Reflex (left and right) and Chronic Red Reflex (left and right). The acute tissue texture changes that the diagnostic staff looked for were warm, moist, inflamed, red, and/or resilient tissue. The chronic tissue texture changes that the diagnostic staff looked for were cold, dry, scaly, itchy, blemished, pale, and/or taut tissue. The quality of tissue texture change was graded on a scale from 0-3. 0 indicated no tissue texture changes, 1 was mild, 2 was moderate, 3 was severe. Findings were also further narrowed down to left versus right.

The **A** section was assessed as hypertonicity (left and right). The amount of asymmetry was graded on a scale from 0-3. 0 indicated no hypertrophy, 1 was mild, 2 was moderate, 3 was severe.

The **R** section assessed for restriction of motion in sidebending, rotation, flexion, and extension for each vertebral unit within T_{10}-L_2 (T_{10}, T_{11}, T_{12}, L_1, and L_2). The quality of motion was graded on a scale from 0-3. 0 indicated no restriction of motion, 1 was mild, 2 was moderate, 3 was severe.

The **T** section was assessing for tenderness at each vertebral unit, T_{10} (left and right), T_{11} (left and right), T_{12} (left and right), L_1 (left and right), and L2 (left and right). Tenderness was assessed based on left versus right side of the vertebral segment and was graded on a scale. The pain scale was used again, where tenderness was rated from 0-10. 0 indicated no tenderness and 10 was the most severe tenderness.

The diagnostic staff was instructed to look for TART changes specifically in the region of T_{10}-L_2, since this is the region that corresponds to a viscerosomatic reflex originating from the kidney. T_{10}-L_2 is the sympathetic innervation region for the renal system. The diagnostic staff was not instructed on how the subject was to be positioned for the palpatory exam. Some of the first few subjects were examined prone, but the majority of the subjects were examined seated. The findings were then recorded on the form entitled "Palpatory Exam Documentation Sheet".

After completing the palpatory exam, the research staff escorted the subjects to the Quest Diagnostics laboratory for the laboratory visit. Quest Diagnostics is located on the first floor of the Patient Care Center at the University of North Texas Health Science Center. Subjects had their blood drawn by a phlebotomist from Quest Diagnostics and submitted a urinalysis for research diagnostic confirmatory purposes.

All subjects submitted a urine sample for analysis. All female subjects also had their urine sample tested with a pregnancy test. If the urine pregnancy test was positive, the subject was dropped from the study and the research staff recommended that the subject make an appointment with their physician. Their data collected was not used, since pregnancy was an exclusionary criterion. It is an exclusionary criterion because subjects must have type 2 diabetes mellitus only (not gestational diabetes), and because the innervation region for the uterus and ovaries is the same innervation region related to the kidney. There is no increased risk related to pregnant females or to the fetus when performing the osteopathic palpatory exam that was used in this research study. However, the inclusion of pregnant individuals would distort the results, making it

difficult to attribute the palpatory findings to diabetic nephropathy. None of the recruited subjects tested positive for pregnancy, therefore no subjects were excluded from the study based on pregnancy.

The remainder of the urine sample was submitted to the Quest Diagnostics laboratory for analysis. The urine sample was analyzed for urine microalbumin creatinine ratio and for urine creatinine level.

Subjects also had their blood drawn by a phlebotomist at Quest Diagnostics. The blood was submitted to the Quest Diagnostics laboratory for analysis. The blood sample was analyzed for a comprehensive metabolic panel (CMP) which determined the subjects' glucose level, BUN, BUN/creatinine ratio, and estimated GFR.

After the laboratory visit, the research staff compensated the subject for their time and inconvenience. Each subject received $15.00 cash.

Data Analysis

The results of the urinalysis and the blood draw were sent to and received by the Osteopathic Research Center. The collected data (subject charts and laboratory work) from all 30 subjects was kept at the Osteopathic Research Center. The copies of the labwork were also sent to the subjects' family physician at the Family Medicine Central Clinic. Only 26 copies of labwork were received by the Osteopathic Research Center. I was unable to locate the missing four copies. Therefore, four subjects were excluded due to incomplete data. A total of 26 subjects' data was reviewed for statistical analysis.

Analysis of the data was conducted using SPSS™ Version 14.0. Chi square analysis and risk assessment was performed on the subjects' data (n=26) to determine if there were any statistically significant associations between palpatory findings and type 2 diabetes mellitus and diabetic nephropathy. Statistical significance was determined using the p value $\alpha < 0.05$.

The results from the "Subjects Demographic Information Sheet", the "Pain Documentation Sheet", and the "Palpatory Exam Documentation Sheet" were used for statistical analysis. The data from the "Subjects Demographic Information Sheet" included gender, age, and race/ethnicity. The gender was recorded as male or female, The age was recorded into two groups: 18-50 and 51-90. The race/ethnicity was recorded as Caucasian or Non-Caucasian. Subjects who documented that their race was Caucasian, their race was recorded in SPSS for analysis as Caucasian. Subjects who documented that their race was Black, Pacific Islander, Native American, Hispanic, or Alaskan Native, their race was recorded in SPSS for analysis as Non-Caucasian.

The data from the "Pain Documentation Sheet" was recorded into two groups: 1 meaning no pain and 0 denoting the subject initially had pain. If the subject documented on the pain scale their pain level as 0, it was recorded in SPSS for analysis as 1. If the subject documented on the pain scale their pain level was 1-10, it was recorded in SPSS for analysis as 0.

The data from the "Palpatory Exam Documentation Sheet" was recorded separately for each TART change palpated.

Tissue texture changes were evaluated in a variety of ways. The palpatory findings were recorded in SPSS into two groups: 1 denoting no change ("none") and 0 denoting there was change ("mild", "moderate", "severe"). First, tissue texture changes were analyzed as general changes within the region of T_{10}-L_2, grouping findings as Left Tissue Texture Change and Right Tissue Texture Change. Then the findings were analyzed as Acute Tissue Texture Change (general, left, and right) and Chronic Tissue Texture Change (general, left, and right). A total of eight different chi square analyses were conducted to compare:1.) control and disease groups and 2.) renal and no renal groups with tissue texture change.

Asymmetry was evaluated as general hypertonicity, left hypertonicity, and right hypertonicity. The palpatory findings were recorded in SPSS into two groups: 1 denoting no hypertrophy ("none") and 0 denoting there was hypertrophy ("mild", "moderate", "severe"). A total of three different chi square analyses were conducted to compare:1.) control and disease groups and 2.) renal and no renal groups with asymmetry.

Restriction of motion was evaluated as general restriction in the area of T_{10}-L_2 and for each segmental vertebral unit (T_{10}, T_{11}, T_{12}, L_1, and L_2). The palpatory findings were recorded in SPSS into two groups: 1 denoting no restriction of motion ("none") and 0 denoting there was restriction of motion ("mild", "moderate", "severe"). A total of six different chi square analyses were conducted to compare:1.) control and disease groups and 2.) renal and no renal groups with restriction of motion.

Tenderness was evaluated as general tenderness in the area of T_{10}-L_2 (left and right) and for each segmental vertebral unit (T_{10} (left and right), T_{11} (left and right), T_{12}

(left and right), L_1 (left and right), and L_2 (left and right)). The palpatory findings were recorded in SPSS into two groups: 1 denoting no tenderness ("0") and 0 denoting there was tenderness ("1-10"). A total of thirteen different chi square analyses were conducted to compare:1.) control and disease groups and 2.) renal and no renal groups with tenderness to palpation.

CHAPTER III

RESULTS

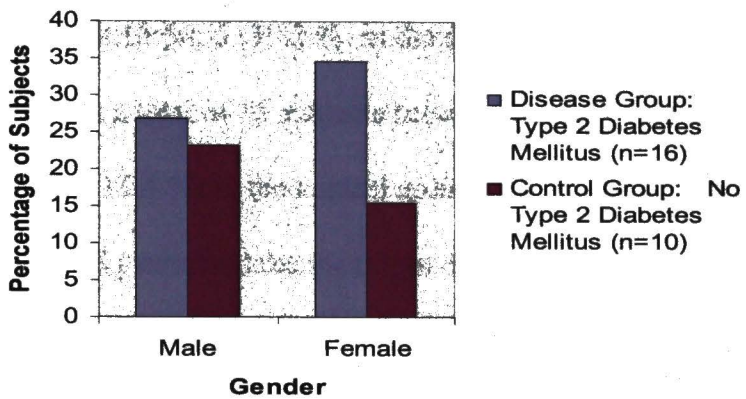
A total of 26 subjects finished the study and had complete data for analysis. The results that were used for analysis were data from the "Subjects Demographic Information Sheet", the "Pain Documentation Sheet", the "Palpatory Exam Documentation Sheet", and labwork. The data was analyzed using SPSS™ Version 14.0 in order to evaluate the validity of each hypothesis.

Hypothesis 1

Hypothesis 1 stated that osteopathic palpatory findings at the thoracolumbar level of T_{10}-L_2 will be more prevalent in subjects with type 2 diabetes mellitus than in subjects without disease. To evaluate the validity of this statement, the data for control and disease subjects were analyzed using descriptive statistics, Chi square analysis, and risk assessment. A P value < 0.05 was used to determine significance.

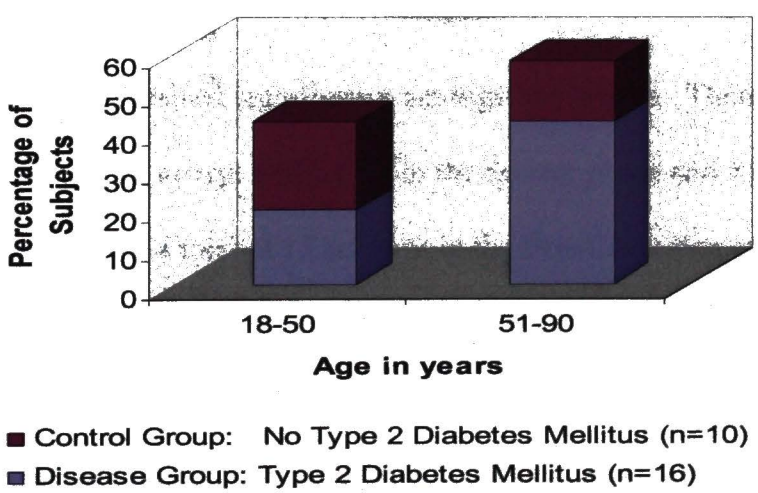
Demographic information (gender, age, and race/ethnicity) was compared with control and disease groups to determine the number of subjects found in each group and to determine if there was any correlation amongst the demographics and the type 2 diabetes mellitus status.

Figure 2: Relationship between gender and control & disease groups



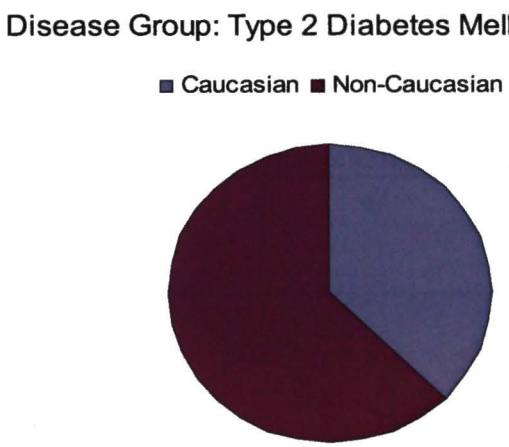
There was no statistical significance found amongst the groups. There were a total of 13 males; 7 (26.9 %) in the disease group and 6 (23.1 %) in the control group. There were a total of 13 females; 9 (34.6 %) in the disease group and 4 (15.4 %) in the control group. The Chi square analysis and risk assessment were calculated to be: χ^2 = 0.650; degrees of freedom (df) = 1; P value = 0.420; odds ratio = 0.519; 95% confidence interval (0.104, 2.581).

Figure 3: Relationship between age and control & disease groups



There was no statistical significance amongst the groups. There were a total of 11 subjects between the ages 18-50; 5 (19.2 %) in the disease group and 6 (23.1 %) in the control group. There was a total of 15 subjects between the ages 51-90; 11 (42.3 %) in the disease group and 4 (15.4 %) in the control group. The minimum age was 18 years, the maximum age was 88 years, and the mean age was 50.93 years. The Chi square analysis and risk assessment were calculated to be: $\chi^2 = 2.084$; df = 1; P value = 0.228; odds ratio = 0.303; 95% confidence interval (0.058, 1.576).

Figure 4: Relationship between race and control & disease groups



There was no statistical significance amongst the groups. There were a total of 11 subjects in the Caucasian group; 6 (23.1 %) in the disease group and 5 (19.2 %) in the control group. There was a total of 15 subjects in the Non-Caucasian group; 10 (38.5 %) in the disease group and 5 (19.2 %) in the control group. The Chi square analysis and risk assessment were calculated to be: $\chi^2 = 0.394$; df = 1; P value = 0.689; odds ratio = 0.600; 95% confidence interval (0.121, 2.973). Although there was not statistical

significance, there is clinical significance. There were more of Non-Caucasian subjects (38.5 %) with type 2 diabetes mellitus than Caucasian subjects (23.1 %).

The palpatory exam findings were compared with control and disease groups to determine the number of subjects found in each group and to determine if there was any correlation amongst the TART changes (tissue texture change, asymmetry, restriction of motion, and tenderness) and the type 2 diabetes mellitus status.

Tissue texture changes were divided into eight groups in SPSS™ Version 14.0 for analysis. There groups were classified as: left tissue texture change, right tissue texture change, acute tissue texture change (general, left, and right), and chronic tissue texture change (general, left, and right).

Table 1: Relationship between tissue texture changes and control & disease groups

Tissue Texture Change	*Disease Group (n=16)*	*Control Group (n=10)*	χ^2	*df*	*P*	*OR*	***95% CI***
Left Tissue Texture Change							
Yes	9 (34.6 %)	5 (19.2 %)	0.097	1	1.000	1.286	0.264
No	7 (26.9 %)	5 (19.2 %)					6.273
Right Tissue Texture Change							
Yes	9 (34.6 %)	7 (26.9 %)	0.492	1	0.683	0.551	0.103
No	7 (26.9 %)	3 (11.5 %)					2.941
Acute Tissue Texture Change							
Yes	9 (34.6 %)	5 (19.2 %)	0.097	1	1.000	1.286	0.264
No	7 (26.9 %)	5 (19.2 %)					6.273
Left Acute Tissue Texture Change							
Yes	7 (26.9 %)	3 (11.5 %)	0.492	1	0.683	1.815	0.340
No	9 (34.6 %)	7 (26.9 %)					9.687
Right Acute Tissue Texture Change							
Yes	2 (7.7 %)	5 (19.2 %)	4.398	1	0.069	0.143	0.021
No	14 (53.8 %)	5 (19.2 %)					0.986
Chronic Tissue Texture Change							
Yes	8 (30.8 %)	4 (15.4 %)	0.248	1	0.701	1.500	0.303
No	8 (30.8 %)	6 (23.1 %)					7.432
Left Chronic Tissue Texture Change							
Yes	4 (15.4 %)	3 (11.5 %)	0.078	1	1.000	0.778	0.133

No	12 (46.2 %)	7 (26.9 %)					4.536
Right Chronic Tissue Texture Change							
Yes	7 (26.9 %)	3 (11.5 %)	0.492	1	0.683	1.815	0.340
No	9 (34.6 %)	7 (26.9 %)					9.687

There was no statistical significance between the tissue texture change variables and type 2 diabetes mellitus status. One variable did show a statistical trend. Right acute tissue texture change approached significance with a P value = 0.069. The Chi square analysis and risk assessment right acute tissue texture change were calculated to be: χ^2 = 4.398; P value = 0.069; odds ratio = 0.143; 95% confidence interval (0.021, 0.986).

Asymmetry was divided into three groups in SPSS™ Version 14.0 for analysis. The three groups were general hypertonicity, left hypertonicity, and right hypertonicity.

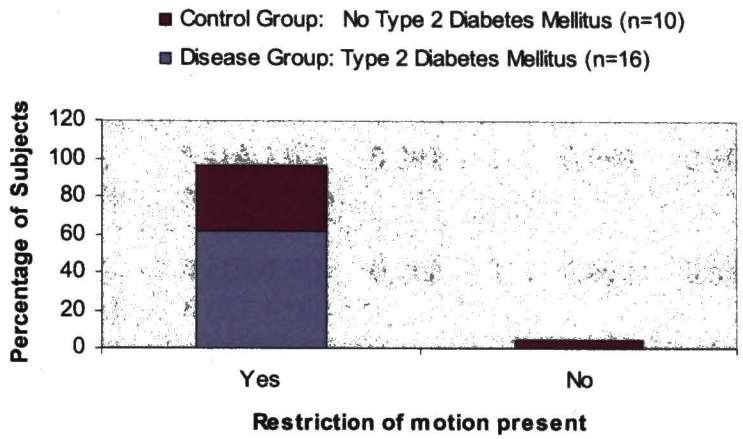
Table 2: Relationship between asymmetry and control & disease groups

Asymmetry	*Disease Group (n=16)*	*Control Group (n=10)*	χ^2	*df*	*P*	*OR*	***95% CI***
Hypertonicity							
Yes	15 (57.7 %)	8 (30.8 %)	1.14	1	0.538	3.750	0.293
No	1 (3.8 %)	2 (7.7 %)	0				47.989
Left Hypertonicity							
Yes	8 (30.8 %)	7 (26.9 %)	1.00	1	0.428	0.429	0.081
No	8 (30.8 %)	3 (11.5 %)	8				2.277
Right Hypertonicity							
Yes	15 (57.7 %)	8 (30.8 %)	1.14	1	0.538	3.750	0.293
No	1 (3.8 %)	2 (7.7 %)	0				47.989

There was no statistical significance found between the asymmetry variables and type 2 diabetes mellitus.

Restriction of motion was divided into six groups in SPSS™ Version 14.0 for analysis. The six groups were divided as general restriction in the area of T_{10}-L_2 and for each segmental vertebral unit (T_{10}, T_{11}, T_{12}, L_1, and L_2).

Figure 5: Relationship between restriction of motion and control & disease groups



All type 2 diabetes mellitus subjects had restriction of motion; there were no type 2 diabetes subjects that did not have restriction of motion. Therefore, odds ratio and risk assessment could not be performed. The data for all six restriction of motion variables were exactly the same. There were a total of 25 subjects with restriction of motion; 16 (61.5 %) in the disease group and 9 (34.6 %) in the control group. There were a total of 1 subject without restriction of motion; 0 (0.0 %) in the disease group and 1 (3.8 %) in the control group. The Chi square analysis was calculated to be: $\chi^2 = 1.664$; df = 1; P value = 0.385. Almost all control and disease subjects had detectable restriction of motion.

Tenderness was divided into thirteen different groups in SPSS™ Version 14.0 for analysis. The thirteen groups were divided as general tenderness in the area of T_{10}-L_2 (left and right) and for each segmental vertebral unit (T_{10} (left and right), T_{11} (left and right), T_{12} (left and right), L_1 (left and right), and L_2 (left and right)).

Table 3: Relationship between tenderness to palpation and control & disease groups

Tenderness to Palpation	*Disease Group(n=16)*	*Control Group(n=10)*	χ^2	*df*	*P*	*OR*	***95% CI***
T_{10}-L_2 Region							
Yes	6 (23.1 %)	5 (19.2 %)	0.394	1	0.689	0.600	0.121
No	10 (38.5 %)	5 (19.2 %)					2.973
Left T_{10}-L_2 Region							
Yes	5 (19.2 %)	4 (15.4 %)	0.208	1	0.692	0.682	0.131
No	11 (42.3 %)	6 (23.1 %)					3.546
Right T_{10}-L_2 Region							
Yes	5 (19.2 %)	4 (15.4 %)	0.208	1	0.692	0.682	0.131
No	11 (42.3 %)	6 (23.1 %)					3.546
Left T_{10}							
Yes	3 (11.5 %)	2 (7.7 %)	0.006	1	1.000	0.923	0.126
No	13 (50.0 %)	8 (30.8 %)					6.781
Right T_{10}							
Yes	2 (7.7 %)	2 (7.7 %)	0.266	1	0.625	0.571	0.067
No	14 (53.8 %)	8 (30.8 %)					4.875
Left T_{11}							
Yes	3 (11.5 %)	2 (7.7 %)	0.006	1	1.000	0.923	0.126
No	13 (50.0 %)	8 (30.8 %)					6.781
Right T_{11}							
Yes	3 (11.5 %)	2 (7.7 %)	0.006	1	1.000	0.923	0.126
No	13 (50.0 %)	8 (30.8 %)					6.781
Left T_{12}							
Yes	4 (15.4 %)	2 (7.7 %)	0.087	1	1.000	1.333	0.196
No	12 (46.2 %)	8 (30.8 %)					9.083
Right T_{12}							
Yes	4 (15.4 %)	2 (7.7 %)	0.087	1	1.000	1.333	0.196
No	12 (46.2 %)	8 (30.8 %)					9.083
Left L_1							
Yes	3 (11.5 %)	2 (7.7 %)	0.006	1	1.000	0.923	0.126
No	13 (50.0 %)	8 (30.8 %)					6.781
Right L_1							
Yes	1 (3.8 %)	2 (7.7 %)	1.140	1	0.538	0.267	0.021
No	15 (57.7 %)	8 (30.8 %)					3.413
Left L_2							
Yes	1 (3.8 %)	3 (11.5 %)	2.666	1	0.264	0.156	0.014
No	15 (57.7 %)	7 (26.9 %)					1.775
Right L_2							
Yes	4 (15.4 %)	2 (7.7 %)	0.087	1	1.000	1.333	0.196
No	12 (46.2 %)	8 (30.8 %)					9.083

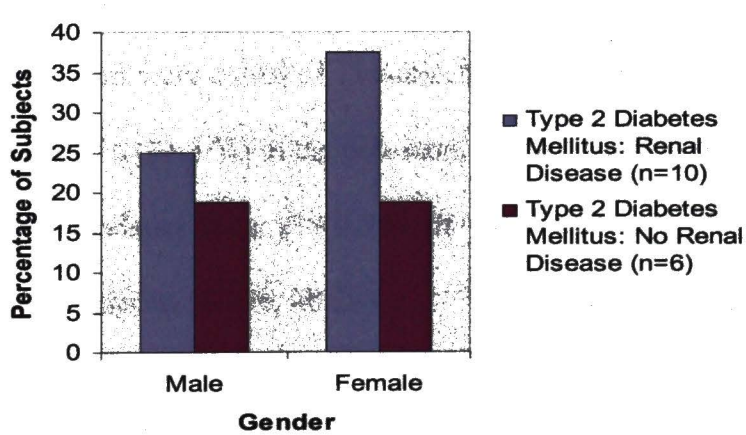
There were no statistically significant findings between tenderness and type 2 diabetes mellitus status. The majority of P values approached 1, indicating that there was no difference between the groups.

Hypothesis 2

Hypothesis 2 stated that osteopathic palpatory findings at the thoracolumbar level of T_{10}-L_2 will be associated with type 2 diabetes mellitus and the development of renal disease. To evaluate the validity of this statement, the data for control and disease subjects were analyzed using descriptive statistics, Chi square analysis, and risk assessment. A p value < 0.05 was used to determine significance.

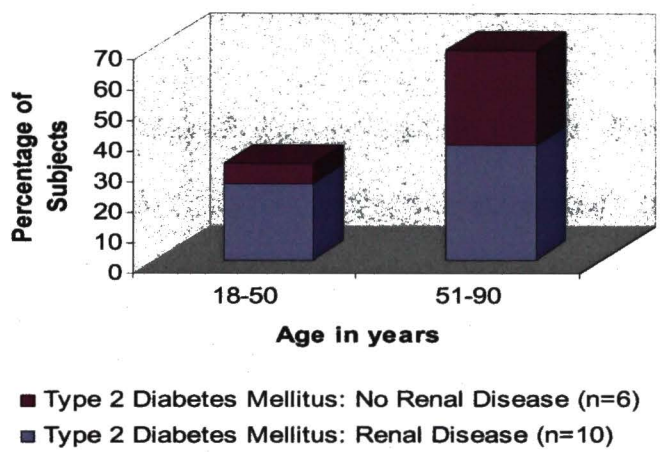
Demographic information (gender, age, and race/ethnicity) was compared with renal and non-renal groups to determine the number of subjects found in each group and to determine if there was any correlation amongst the demographics and the renal disease status.

Figure 6: Relationship between gender and renal & non-renal groups



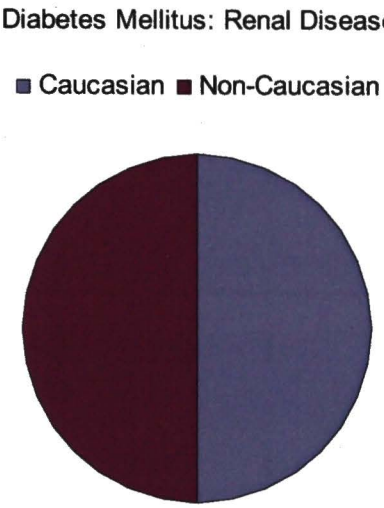
There was no statistical significance found amongst the groups. There were a total of 7 males; 4 (25.0 %) in the renal group and 3 (18.8 %) in the non-renal group. There were a total of 9 females; 6 (37.5 %) in the renal group and 3 (18.8 %) in the non-renal group. The Chi square analysis and risk assessment were calculated to be: χ^2 = 0.152; df = 1; P value = 1.000; odds ratio = 0.667; 95% confidence interval (0.087, 5.127).

Figure 7: Relationship between age and renal & non-renal groups



There was no statistical significance found amongst the groups. There were a total of 5 subjects between the ages 18-50; 4 (25.0 %) in the renal group and 1 (6.3 %) in the non-renal group. There were a total of 11 subjects between the ages 51-90; 6 (37.5 %) in the renal group and 5 (31.3 %) in the non-renal group. The Chi square analysis and risk assessment were calculated to be: χ^2 = 0.950; df = 1; P value = 0.588; odds ratio = 3.333; 95% confidence interval (0.276, 40.287).

Figure 8: Relationship between race and renal & non-renal groups



There was no statistical significance amongst the groups. There were a total of 6 subjects in the Caucasian group; 5 (31.3 %) in the renal group and 1 (6.3 %) in the non-renal group. There was a total of 10 subjects in the Non-Caucasian group; 5 (31.3 %) in the renal group and 5 (31.3 %) in the non-renal group. The Chi square analysis and risk assessment were calculated to be: $\chi^2 = 1.778$; df = 1; P value = 0.307; odds ratio = 5.000; 95% confidence interval (0.419, 59.657).

The palpatory exam findings were compared with renal and non-renal groups to determine the number of subjects found in each group and to determine if there was any correlation amongst the TART changes (tissue texture change, asymmetry, restriction of motion, and tenderness) and the renal disease status.

Tissue texture changes were divided into eight groups in SPSS™ Version 14.0 for analysis. There groups were classified as: left tissue texture change, right tissue texture

change, acute tissue texture change (general, left, and right), and chronic tissue texture change (general, left, and right).

Table 4: Relationship between tissue texture changes and renal & non-renal groups

Tissue Texture Change	*Renal Disease (n=10)*	*No Renal Disease (n=6)*	χ^2	*df*	*P*	*OR*	***95% CI***
Left Tissue Texture Change							
Yes	6 (37.5 %)	3 (18.8 %)	0.152	1	1.000	1.500	0.195
No	4 (25.0 %)	3 (18.8 %)					11.536
Right Tissue Texture Change							
Yes	4 (25.0 %)	5 (31.3 %)	2.861	1	0.145	0.133	0.011
No	6 (37.5 %)	1 (6.3 %)					1.611
Acute Tissue Texture Change							
Yes	7 (43.8 %)	2 (12.5 %)	2.049	1	0.302	4.667	0.533
No	3 (18.8 %)	4 (25.0 %)					40.886
Left Acute Tissue Texture Change							
Yes	4 (25.0 %)	1 (6.3 %)	2.861	1	0.145	7.500	0.621
No	6 (37.5 %)	5 (31.3 %)					90.646
Right Acute Tissue Texture Change							
Yes	1 (6.3 %)	1 (6.3 %)	0.152	1	1.000	0.556	0.028
No	9 (56.3 %)	5 (31.3 %)					10.933
Chronic Tissue Texture Change							
Yes	4 (25.0 %)	4 (25.0 %)	1.067	1	0.608	0.333	0.040
No	6 (37.5 %)	2 (12.5 %)					2.769
Left Chronic Tissue Texture Change							
Yes	2 (12.5 %)	2 (12.5 %)	0.356	1	0.604	0.500	0.050
No	8 (50.0 %)	4 (25.0 %)					4.978
Right Chronic Tissue Texture Change							
Yes	3 (18.8 %)	4 (25.0 %)	2.049	1	0.302	0.214	0.024
No	7 (43.8 %)	2 (12.5 %)					1.877

There was no statistical significance between the tissue texture change variables and type 2 diabetes mellitus status. Two variables did show a trend toward. Right tissue texture change and left acute tissue texture change approached significance with a P value = 0.145 for both. The Chi square analysis and risk ratio right tissue texture change were calculated to be: $\chi^2 = 2.861$; P value = 0.145; odds ratio = 0.133; 95% confidence

interval (0.011, 1.611). The Chi square analysis and risk assessment left acute tissue texture change were calculated to be: $\chi^2 = 2.861$; P value = 0.145; odds ratio = 7.500; 95% confidence interval (0.621, 90.646).

Asymmetry was divided into three groups in SPSS™ Version 14.0 for analysis. The three groups were general hypertonicity, left hypertonicity, and right hypertonicity.

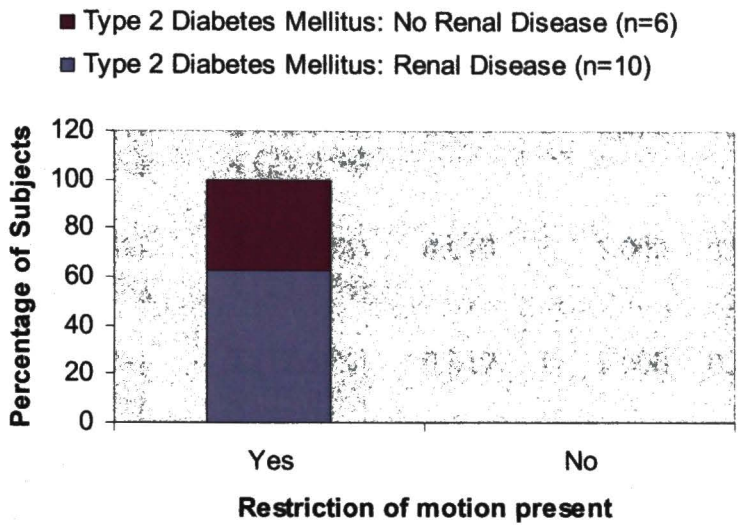
Table 5: Relationship between asymmetry and renal & non-renal groups

Asymmetry	*Renal Disease (n=10)*	*No Renal Disease (n=6)*	χ^2	*df*	*P*	*OR*	***95% CI***
Hypertonicity							
Yes	9 (56.3 %)	6 (37.5 %)	0.640	1	1.000		
No	1 (6.3 %)	0 (0.0 %)					
Left Hypertonicity							
Yes	6 (37.5 %)	2 (12.5 %)	1.067	1	0.608	3.000	0.361
No	4 (25.0 %)	4 (25.0 %)					24.919
Right Hypertonicity							
Yes	9 (56.3 %)	6 (37.5 %)	0.604	1	1.000		
No	1 (6.3 %)	0 (0.0 %)					

There was no statistical significance found between the asymmetry variables and renal disease. Odds ratio and risk assessment were not calculated for hypertonicity and right hypertonicity variables because at least one category had no subjects.

Restriction of motion was divided into six groups in SPSS™ Version 14.0 for analysis. The six groups were divided as general restriction in the area of T_{10}-L_2 and for each segmental vertebral unit (T_{10}, T_{11}, T_{12}, L_1, and L_2).

Figure 9: Relationship between restriction of motion and renal & non-renal groups



All renal disease subjects had restriction of motion; there were no renal disease subjects that did not have restriction of motion. The data for all six restriction of motion variables were exactly the same. There were a total of 16 subjects with restriction of motion; 10 (62.5 %) in the renal group and 6 (37.5 %) in the non-renal group. There were no subjects without restriction of motion; 0 (0.0 %) in the renal group and 0 (0.0 %) in the non-renal group. The Chi square analysis and risk assessment were not performed because restriction of motion was considered to be a constant. All renal and non-renal disease subjects had detectable restriction of motion.

Tenderness was divided into thirteen different groups in SPSS™ Version 14.0 for analysis. The thirteen groups were divided as general tenderness in the area of T_{10}-L_2 (left and right) and for each segmental vertebral unit (T_{10} (left and right), T_{11} (left and right), T_{12} (left and right), L_1 (left and right), and L_2 (left and right)).

Table 6: Relationship between tenderness to palpation and renal & non-renal groups

Tenderness to Palpation	*Renal Disease(n=10)*	*No Renal Disease(n=6)*	χ^2	df	*P*	*OR*	***95% CI***
T_{10}-L_2 Region							
Yes	4 (25.0 %)	2 (12.5 %)	0.071	1	1.000	1.333	0.161
No	6 (37.5 %)	4 (25.0 %)					11.075
Left T_{10}-L_2 Region							
Yes	3 (18.8 %)	2 (12.5 %)	0.019	1	1.000	0.857	0.098
No	7 (43.8 %)	4 (25.0 %)					7.510
Right T_{10}-L_2 Region							
Yes	3 (18.8 %)	2 (12.5 %)	0.019	1	1.000	0.857	0.098
No	7 (43.8 %)	4 (25.0 %)					7.510
Left T_{10}							
Yes	2 (12.5 %)	1 (6.3 %)	0.027	1	1.000	1.250	0.089
No	8 (50.0 %)	5 (31.3 %)					17.653
Right T_{10}							
Yes	1 (6.3 %)	1 (6.3 %)	0.152	1	1.000	0.556	0.028
No	9 (56.3 %)	5 (31.3 %)					10.933
Left T_{11}							
Yes	2 (12.5 %)	1 (6.3 %)	0.027	1	1.000	1.250	0.089
No	8 (50.0 %)	5 (31.3 %)					17.653
Right T_{11}							
Yes	1 (6.3 %)	2 (12.5 %)	1.340	1	0.518	0.222	0.015
No	9 (56.3 %)	4 (25.0 %)					3.221
Left T_{12}							
Yes	2 (12.5 %)	2 (12.5 %)	0.356	1	0.604	0.500	0.050
No	8 (50.0 %)	4 (25.0 %)					4.978
Right T_{12}							
Yes	2 (12.5 %)	2 (12.5 %)	0.356	1	0.604	0.500	0.050
No	8 (50.0 %)	4 (25.0 %)					4.978
Left L_1							
Yes	1 (6.3 %)	2 (12.5 %)	1.340	1	0.518	0.222	0.015
No	9 (56.3 %)	4 (25.0 %)					3.221
Right L_1							
Yes	1 (6.3 %)	0 (0.0 %)	0.640	1	1.000		
No	9 (56.3 %)	6 (37.5 %)					
Left L_2							
Yes	1 (6.3 %)	0 (0.0 %)	0.640	1	1.000		
No	9 (56.3 %)	6 (37.5 %)					
Right L_2							
Yes	3 (18.8 5)	1 (6.3 %)	0.356	1	1.000	2.143	0.169
No	7 (43.8 %)	5 (31.3 %)					27.103

There were no statistically significant findings between tenderness and type 2 diabetes mellitus status. The majority of P values approached 1, indicating that there was no difference between the groups. Odds ratio and risk assessment were not performed for Right L_1 and Left L_2 because at least one category had no subjects.

The initial pain measured by subjects was also analyzed. Initial pain was compared with control and disease groups. There were no statistically significant findings between initial pain and type 2 diabetes mellitus status. There were a total of 9 subjects who documented pain prior to exam; 6 (23.1 %) in the disease group and 3 (11.5 %) in the control group. There was a total of 17 subjects who did not have pain prior to exam; 10 (38.5 %) in the disease group and 7 (26.9 %) in the control group. The Chi square analysis and risk assessment were calculated to be: $\chi^2 = 0.153$; df = 1; P value = 1.000; odds ratio = 1.400; 95% confidence interval (0.259, 7.582).

Initial pain was compared with renal and non-renal groups. There were no statistically significant findings between initial pain and renal status. There were a total of 6 subjects who documented pain prior to exam; 5 (31.3 %) in the renal group and 1 (6.3 %) in the non-renal group. There was a total of 10 subjects who did not have pain prior to exam; 5 (31.3 %) in the renal group and 5 (31.3 %) in the non-renal group. The Chi square analysis and risk assessment were calculated to be: $\chi^2 = 1.778$; df = 1; P value = 0.307; odds ratio = 5.000; 95% confidence interval (0.419, 59.657).

Initial pain was also compared with tenderness to palpation on exam. There was a statistical trend towards significance between initial pain and tenderness on palpation. There were a total of 11 subjects who documented pain prior to exam; 6 (23.1 %) in the

disease group and 5 (19.2 %) in the control group. There was a total of 15 subjects who did not have pain prior to exam; 3 (11.5 %) in the disease group and 12 (46.2 %) in the control group. The Chi square analysis and risk assessment were calculated to be: χ^2 = 3.346; df = 1; P value = 0.103; odds ratio = 4.800; 95% confidence interval (0.847, 27.202).

CHAPTER IV

DISCUSSION

None of the results from this study proved to be statistically significant. There were a few variables that were either clinically relevant and or demonstrated a trend toward significance.

There were some variables that proved important in comparing demographic information and palpatory findings with type 2 diabetes mellitus. According to previous research, there is a correlation between type 2 diabetes mellitus and race. The National Diabetes Association states that in individuals twenty years of age and older, non-Hispanic blacks and Hispanics are more likely to develop type 2 diabetes mellitus.[1] Based upon this study, non-Caucasian subjects were more likely to have type 2 diabetes mellitus than Caucasian subjects. 38.5% of subjects were non-Caucasian and had diabetes as opposed to 23.1% of subjects who were Caucasian and had diabetes. The P value for the race variable is 0.689, which is neither statistically significant nor trending toward significance.

This correlation between race and type 2 diabetes mellitus is extremely important to the physician. Understanding that a relationship exists proves to be clinically significant because it provides the physician with the ability to identify those individuals

who are at high risk for developing disease. Known risk factors for developing type 2 diabetes mellitus include obesity, family history, older age, history of gestational diabetes, physical inactivity, impaired fasting glucose, and race/ethinicity.[1] Risk factors does not mean that disease will only occur in people who have these factors. Instead, identification of risk factors raises clinical suspicion for disease and helps identify individuals who are more apt to develop disease. Therefore, paying close attention to risk factors is one method of screening patients for a particular disease, and will hopefully help implement early intervention in order to deter disease development.

Tissue texture changes have been suggested by some to have a strong correlation with disease, and more specifically with a viscerosomatic reflex. According to Licciardone *et al.*, there was a significant association between tissue change (doughy, ropy, thickened, and/or fibrotic tissue) at the level of T_{11}-L_2 and type 2 diabetes mellitus.[21] The results provided by the current study demonstrated evidence to the contrary. All of the tissue texture change variables were not statistically significant; but, one variable demonstrated a trend towards significance.

Right acute tissue texture change had a P value of 0.069. Out of the 16 disease group subjects, 14 (53.8%) did not have right acute tissue texture change while 2 (7.7%) did have this TART change. Therefore, this study showed a trend that those subjects with type 2 diabetes mellitus were more likely to not have right acute tissue texture change. The odds ratio was 0.143 and the 95% confidence interval was 0.021, 0.986. An odds ratio less than 1 and a 95% confidence interval that did not contain 1 may be interpreted as a negative association between type 2 diabetes mellitus and right acute

tissue texture change at the 5% significance level. The odds of having right acute tissue texture change and type 2 diabetes mellitus is smaller than having this change and not having diabetes. Meaning that it is more likely for control group subjects to have right acute tissue texture change than diabetic subjects.

This result was surprising. I had expected to find statistical significance or a trend toward significance indicating that tissue texture change was more likely to be associated with type 2 diabetes than in control subjects. This result may be due to the small number of subjects who participated in the study. Perhaps a larger amount of subjects would have provided a different result. But, I think this outcome occurred because type 2 diabetes mellitus is a chronic disease. The TART finding was right *acute* tissue texture change. The palpatory findings associated with acute and chronic somatic dysfunction are different. Acute somatic dysfunction manifests as doughy, boggy tissue, hyperesthesia, increase in skin temperature, increase in moisture, increase in skin drag, an increase in subcutaneous fluid, diffuse muscle contraction, and thickening of the skin texture.[22, 32] Chronic somatic dysfunction manifests as more pronounced thickening of the skin and subcutaneous tissue, localized muscle contraction, deep muscle splinting, abnormal hardness and rigidity, absence of hypesthesia, and a decrease in motion.[22, 32] If a viscerosomatic reflex was present at the level of T_{10}-L_2, then type 2 diabetes mellitus subjects had not yet developed somatic manifestations of the disease process or the disease was not acute in nature.

There were some variables that proved important in comparing demographic information and palpatory findings with subjects' renal disease status. As mentioned

previously, Licciardone *et al.* identified an association between tissue texture changes at T_{11}-L_2 and type 2 diabetes mellitus.[21] The conclusion from that study was that these changes at T_{11}-L_2 were a result of a viscerosomatic reflex originating from the kidney, and possibly was due to diabetic nephropathy.[21] Johnston *et al.* found that in subjects with renal failure, the most common palpatory findings was tissue texture change (increase in skin temperature) in the region of T_9-T_{12}.[22, 39] The results provided by the current study demonstrated evidence to the contrary. The results did not demonstrate any statistically significant findings between TART changes and renal disease; but, there were two variables that showed a trend toward significance.

Right tissue texture change and left acute tissue texture change approached significance with a P value of 0.145. For right tissue texture change, there were a total of 10 disease subjects who had renal disease; 4 (25%) did have right tissue texture change and 6 (37.5%) did not have the palpatory finding. Therefore, this study seemed showed a trend that those subjects with renal disease were more likely to not have right acute tissue texture change. The odds ratio for right tissue texture change was 0.133 and the 95% confidence interval was 0.011, 1.611. An odds ratio less than 1 and a 95% confidence interval that did contain 1 may be interpreted as an association between right tissue texture change and renal disease status was not proven at the 5% significance level.

For left acute tissue texture change, 4 (25.0%) did have left acute tissue texture change and 6 (37.5%) did not have the TART change. Therefore, this study seemed showed a trend that those subjects with renal disease were more likely to not have right acute tissue texture change. The odds ratio for left acute tissue texture change was 7.500

and the 95% confidence interval was 0.621, 90.646. An odds ratio greater than 1 and a 95% confidence interval that did contain 1 may be interpreted as an association between left acute tissue texture change and renal disease status was not proven at the 5% significance level.

Given information from previous research studies, both of these results were not expected. I had anticipated finding statistical significance or a trend toward significance indicating that tissue texture change was more likely to be associated with renal disease subjects than in non-renal disease subjects. Although these results suggest a trend toward significance, a larger sample size could more definitively determine whether there is or is not significance between left acute and right tissue texture change and renal disease status. The confidence interval for both palpatory findings suggests that there is no relationship; but, a larger number of subjects could provide a more definitive answer.

Besides sample size and acuity vs. chronicity of the disease accounting for the statistical findings, there are other factors that may account for the lack of tissue texture changes found in relation to the presence of disease. They are glucose neurotoxicity, use of reno-protective medications, the control status of type 2 diabetes mellitus and hypertension, and the timing of the screening.

Type 2 diabetes mellitus is a neurotoxic disease process. Many patients develop neuropathy, namely peripheral neuropathy, as a long term sequelae of the disease. Prolonged elevated levels of glucose will ultimately result in neuronal damage as a result of intracellular glucose metabolism.[40] This phenomena of diabetic neuropathy has readily been studied relating to the effects glucose has on the nervous innervation in the

extremities. Therefore, we can postulate that hyperglycemia has the same effects on all nervous tissue, including afferent and efferent nerves in the spinal reflex arcs that contribute to a viscerosomatic reflex. If neurotoxicity develops in the afferent and efferent nerves of the spinal cord, then the transmission of information from diseased visceral organs to somatic tissue will be dampened or non-existent. Without such neuronal information, a viscerosomatic reflex will not develop and somatic dysfunction, resulting in a palpatory change will not occur.

As mentioned previously, the use of anti-hypertensive medications and glycemic agents are the mainstay of diabetic therapy. Using these medications is essential to diminish and deter the effects angiotensin II and glucose has on the body, namely the renal system. Therefore, early intervention and continual use of the medications will preserve renal function. I did not assess whether or not subjects were on reno-protective medications or for how long they were on the medications. Obtaining this information would have been useful to determine if it had any affect on the presence or absence of TART palpatory changes. Theoretically, being on anti-hypertensives and glycemic agents should decrease the amount of renal damage and, therefore, decrease the amount of viscerosomatic reflexes that are present as a result of the development of nephropathy. Also, I did not assess for how long individuals had type 2 diabetes mellitus, whether their diabetes was controlled or uncontrolled, if they had hypertension, and whether or not their hypertension was controlled or uncontrolled. Assessing these factors would also help to understand whether or not acuity/chronicity or controlled/uncontrolled disease

would affect the presence or absence of somatic manifestations of viscerosomatic reflexes.

Screening for diabetic nephropathy occurs early in the disease process; stage 3 "incipient nephropathy" out of the 5 stages outlined by Remuzzi *et al.*[9] During the "incipient nephropathy" stage, microscopic damage to the renal system is occurring. Therefore, the disease of diabetic nephropathy has not fully developed. All of the subjects in this study who were considered to have diabetic nephropathy had minimally elevated renal markers, also signifying that they had minimal renal damage. In fact, all of the renal disease subjects did not have an official clinical diagnosis of diabetic nephropathy. They were considered to be in the renal disease group based upon laboratory data that indicated there was some sort of renal impairment. If the development of diabetic nephropathy was still in its infancy ('incipient nephropathy'), then the renal changes may not have been strong enough to fully elicit a stimulus that would create a viscerosomatic reflex. If this was the case, then the somatic manifestation of the viscerosomatic reflex would not have yet become apparent. Future work in this area should focus on subjects who more definitively have diabetic nephropathy and renal impairment. This would allow time for the diseased renal system to send a strong enough stimulus to the dorsal horn, converge, cause facilitation, incite a viscerosomatic reflex, and create somatic dysfunction in the form of TART changes that would be apparent on palpation. It would also be interesting to compare those with microalbuminuria and macroalbuminuria to see if there was any difference amongst those with minimal renal damage and more advanced renal damage and the development of somatic dysfunction.

Prior research identified specific TART changes that are typically found with a viscerosomatic reflex. Tissue texture change is one such TART change that has been linked to viscerosomatic changes. It has been found to be the most noteworthy marker for identifying viscerosomatic reflexes.[22] Another TART change that has been previously mentioned in research is for its relationship with a viscerosomatic reflex is restriction of motion. Restriction of motion has been found to be least indicative for the presence of a viscerosomatic reflex. [22] Based upon the findings from this current study, I have to agree with this negative association.

In comparing restriction of motion and type 2 diabetes mellitus status, there was not much difference between the two groups. Out of 16 disease group subjects, 16 (61.5%) had restriction of motion at T_{10}-L_2 and 0 (0.0%) did not have restriction of motion. Out of 10 control group subjects, 9 (34.6%) had restriction of motion and 1 (3.8%) did not have restriction of motion. There were a total of six variables for restriction of motion; all six variables had the same descriptive information, the same Chi square analysis, and P value. Odds ratio and risk assessment were not performed since one of the categories had no subjects. The P value for restriction of motion was 0.385. Although this value is not statistically significant, I think it has clinical relevance. There seems to be no difference amongst those subjects with and without type 2 diabetes mellitus. Almost all subjects had restriction of motion. Therefore, in the clinical setting the use of restriction of motion is not a reliable marker for determining the presence or absence of a viscerosomatic reflex.

In comparing restriction of motion and renal disease status, there was absolutely no difference between the two groups. Out of 10 renal disease subjects, 10 (62.5%) had restriction of motion at T_{10}-L_2 and 0 (0.0%) did not have restriction of motion. Out of 6 non-renal subjects, 6 (37.5%) had restriction of motion at T_{10}-L_2 and 0 (0.0%) did not have restriction of motion. Chi square analysis, odds ratio, and risk assessment were not performed because restriction of motion was viewed as a constant; there were no subjects who did not have restriction of motion. There seems to be no difference amongst those subjects with and without renal disease. All subjects had restriction of motion. Therefore, in the clinical setting the use of restriction of motion is not a reliable marker for determining the presence or absence of a viscerosomatic reflex.

The remaining TART changes evaluated were asymmetry and tenderness to palpation. Both of these palpatory findings proved to not be statistically significant. In fact, the P values for the variables were 1.000 or approached 1.000. This implies that the groups (type 2 diabetes status and asymmetry/tenderness to palpation; renal disease status and asymmetry/tenderness to palpation) are identical and that there is not difference.

Although tenderness to palpation did not have any statistical significance in the relationship between type 2 diabetes mellitus status and renal disease status, there was a trend toward significance in comparing those who initially had pain and tenderness to palpation. The P value for tenderness to palpation on exam compared with initial pain was 0.103. Out of 17 subjects who did not have pain prior to exam, 5 (19.25) had tenderness to palpation and 12 (46.2%) did not have tenderness to palpation. This implies that those subjects who initially did not complain of pain were not tender on

exam; and, those who did initially complain of pain were tender on exam. The odds ratio was 4.800 and the 95% confidence interval was 0.847, 27.202. An odds ratio greater than 1 and a 95% confidence interval that does include 1 indicate that an association between initial pain and tenderness to palpation was not proven at the 5% significance level.

CHAPTER V

CONCLUSION AND LIMITATIONS

The purpose of this study was to evaluate if there was an association between osteopathic palpatory findings and type 2 diabetes mellitus and diabetic nephropathy. Previous research has already established a connection between visceral activity and somatic activity. The viscerosomatic reflex occurs when the viscera sends a stimulus to the dorsal horn of the spinal cord, convergence and facilitation occur, and then an efferent impulse is sent to the somatic tissue.[22-25, 27] What occurs as a result of this efferent somatic impulse has yet to be fully elucidated. Speculation is that the somatic tissue will react and change, manifesting in somatic dysfunction. Somatic dysfunction may represent itself in the soma as TART changes (tissue texture changes, asymmetry, restriction of motion, and tenderness to palpation). Tissue texture change, namely increase in skin temperature, has been found to be the most common somatic manifestation of a viscerosomatic reflex.[21, 22, 39] Restriction of motion has been found to be the least likely to correlate with visceral activity.[22] Establishing a palpatory connection between visceral activity and somatic tissue may help in screening for and diagnosing disease.

Of all the TART changes evaluated in this study, I had been expecting there to be a positive association between both type 2 diabetes mellitus and tissue texture change and

between renal disease and tissue texture change. I had expected these results because previous research indicated that there was a strong correlation. Unfortunately, the results from this study did not support this. Neither of the hypotheses outlined in this study were able to be validated.

Hypothesis 1 stated that palpatory findings at the thoracolumbar level of T_{10}-L_2 will be more prevalent in subjects with type 2 diabetes mellitus than in subjects without disease. According to the results of this study, there were not statistically significant data that supported this claim. There was a trend toward significance with the TART change, right acute tissue texture change. The trend toward significance implied that there was a negative association between right acute tissue texture changes and type 2 diabetes mellitus; those with type 2 diabetes mellitus were more likely to not have right acute tissue texture change.

Hypothesis 2 states that palpatory findings at the thoracolumbar level of T_{10}-L_2 will be associated with type 2 diabetes mellitus and the development of renal disease. According to the results of this study, there were not statistically significant data that supported this claim. The two tissue texture change variables that seemed to trend toward significance both showed, based upon odds ratio and 95% confidence interval, that an association between renal disease and no renal disease could not be proven.

Despite not being able to validate my hypotheses, I believe this was a well designed study and executed well. There were several factors that limited the progress of this study, and may be categorized as external and internal factors.

The external factors that limited this study include both time duration of the study and number of subjects. This study ran from March 2007 to April 2007 and began again in August 2007 and ended November 2007. There was a break from April 2007 until August 2007 because there was no one in the Osteopathic Manipulative Medicine department who was able to perform recruitment during those months. Within the 6 months the study was actively running, a total of 30 subjects were recruited. The research staff who conducted the recruiting was only able to do so for a half day once or twice a week. The amount of time spent in the Family Medicine Central Clinic was limited and screening a large group of potential subjects was minimal. Had there been more time available and more staff able to assist in recruitment, there would have been more subjects enrolled. A larger number of participants would have increased the likelihood of having statistical significance with some of the variables. If there was a larger amount of subjects who participated in the study, I could have conducted more in depth statistical analyses, such as regression model and multivariate analysis, in order to control for age and race. I also would have liked to have done a recruitment rate for this project in order to keep track of how many potential subjects we approached and how many charts we reviewed.

Given the small number of recruited subjects, I had to exclude four subjects because their data was not complete. These subjects fully participated in the study and qualified based upon inclusion and exclusion criteria, but were ultimately excluded because the laboratory work from Quest Diagnostics laboratory was missing. Despite trying very hard to locate the labwork results, I could not; therefore, I had to exclude

them from the study because I could not accurately divide them into any of the groups or subgroups.

The internal factors that limited this study include study design and the palpatory exam. I think the overall design of the study was very well done, but probably too complex for my first research project and for the amount of time available. Having to screen and recruit for three groups (control subjects, type 2 diabetes subjects, and renal disease subjects) proved to be cumbersome. I think it would have been easier to just screen for renal and non-renal subjects. The main focus of this study was to determine if palpatory findings were associated with the development of diabetic nephropathy. Out of the 26 subjects who were included in the study, only 10 subjects had renal disease. Having such a small number of subjects in the renal disease group greatly limited the amount of statistical analysis that could be done and ultimately did not demonstrate any significance in relation to palpatory TART changes. Focusing recruitment on renal disease subjects would have increased the number of these subjects who participated and would have increased the likelihood of finding a statistically significant result.

Another internal factor that limited this study was the palpatory exam. Now realizing that asymmetry, tenderness to palpation, and restriction of motion are not likely to play a role in the somatic manifestation of a viscerosomatic reflex, I probably would not have included them in the palpatory exam. Instead I would have focused my attention on tissue texture changes. I would have evaluated tissue texture change as individual factors, instead of lumping the different types of changes into two main groups (acute and chronic change). For example, I would have had the diagnostic staff evaluate

the temperature and record results, evaluate the texture of the tissue and record results, evaluate the trophic changes and record results, etc. Conducting the physical examination in such a manner would have focused the examiners attention on specific factors instead of evaluating the area for general factors of change.

Another aspect of the palpatory exam that limited this study was the interrater reliability of the diagnostic staff. The diagnostic staff who conducted the palpatory exam consisted of two third year osteopathic manipulative medicine students who are participating in the pre-doctoral fellowship with the osteopathic manipulative medicine department. Although they were similarly trained on how to conduct the palpatory exam, the majority of the exam was based on their ability to grade degrees of somatic dysfunction (ie: mild, moderate, severe palpatory change). There was no training is what was to be considered "mild" or "moderate" or "severe", therefore there was a lot of subjectivity to the documentation of the presence of a palpatory exam. Future studies should focus on in depth training for those who conduct the palpatory exam or even have individuals who are more experienced conduct the exam. Doing so may provide a more object manner of assessing palpatory change.

I believe this study was a success, despite these limitations and the fact that I was not able to prove or disprove my hypotheses. Even though the results of this study seem to want to indicate that there is a negative association between disease status and tissue texture change, I do not believe such an association exists. There has been plenty of research conducted that has shown there to be a positive correlation between tissue texture change and disease.

In this study, a statistically significant result may not have occurred because of the small number of subjects who participated, acuity vs. chronicity of the disease, glucose neurotoxicity, the use of reno-protective medications, control status of type 2 diabetes mellitus and hypertension, and because the disease of diabetic nephropathy had not fully developed in these subjects.

Based on this realization, I would not recommend palpatory TART changes as a screening tool for the development of diabetic nephropathy independent of other methods of screening. Instead, I would recommend the use of palpation to aid in diagnosis of underlying disease. Physicians should always look at the patients' skin, palpate tissue, and assess for TART changes as common practice. In doing so, clinicians may identify abnormalities that were otherwise overlooked. There are three important clinical correlations that I will take from this project: race is associated with an increased likelihood of developing diabetes mellitus and diabetic nephropathy; based on previous research, tissue texture change (increase in skin temperature) has been found to be the most common palpatory finding of somatic dysfunction that is associated with a viscerosomatic reflex; but based on my research hands-on palpatory assessment of tissue texture changes may not clearly distinguish between those with disease and those without, and restriction of motion is the least likely TART change to indicate the presence or absence of a viscerosomatic reflex.

APPENDIX

The Use of Osteopathic Palpatory Findings in Screening for Nephropathy in Type 2 Diabetes Mellitus: A Pilot Study

Principal Investigator: John Licciardone D.O., M.S., M.B.A
Co-Investigator: Laura Curlee MS4

Recruitment Screening Form – Research Staff
Control Group

Yes No

Does the medical record have a signed "Acknowledgement of Receipt of Notice of Privacy Practices" form?

Is the subject subject older than 18 years?

Does the subject have a current diagnosis of Type 2 Diabetes Mellitus?

Does the subject have a current diagnosis of Type 1 Diabetes Mellitus?

Does the subject have a Past Medical History of any of the following diseases?

Crohn's disease Ulcerative colitis

Conn's syndrome Addison's disease

Cushing's syndrome Irritable bowel syndrome

Prostatitis Pelvic inflammatory disease

Benign prostatic hypertrophy

Is the subjects' most recent blood sugar glucose level less than 126 mg/dl? Please document the blood sugar glucose level and date below:

_____ DATE

_____ BLOOD SUGAR GLUCOSE

The Use of Osteopathic Palpatory Findings in Screening for Nephropathy in Type 2 Diabetes Mellitus: A Pilot Study

Principal Investigator: John Licciardone D.O., M.S., M.B.A
Co-Investigator: Laura Curlee MS4

Recruitment Screening Form – Research Staff
Disease Group

Yes No

Does the medical record have a signed "Acknowledgement of Receipt of Notice of Privacy Practices" form?

Is the subject older than 18 years of age?

Does the subject have a current diagnosis of Type 2 Diabetes Mellitus?

Does the subject have a current diagnosis of Type 1 Diabetes Mellitus?

Does the subject have a Past Medical History of any of the following diseases?

Crohn's disease Ulcerative colitis

Conn's syndrome Addison's disease

Cushing's syndrome Irritable bowel syndrome

Prostatitis Pelvic inflammatory disease

Benign prostatic hypertrophy

What is the subjects' most recent urinary microalbumin level?
Please document the urinary microalbumin level and date below:

_____ _____

DATE URINARY MICROALBUMIN

The Use of Osteopathic Palpatory Findings in Screening for Nephropathy in Type 2 Diabetes Mellitus: A Pilot Study

Principal Investigator: John Licciardone D.O., M.S., M.B.A
Co-Investigator: Laura Curlee MS4

Recruitment Screening Form - Subject

Subject Identification Number: _____

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1. Are you older than 18 years of age? yes no

2. Have you been diagnosed with Diabetes Mellitus? yes no

   If yes, which type?

   Type 1 Diabetes Mellitus Type 2 Diabetes Mellitus

3. Are you currently pregnant? yes no N/A

   When was your last normal menstrual period? _____

4. In the past year, have you been pregnant? yes no N/A

5. Do you have known kidney disease? yes no

   If yes, what type?_____

6. In the past year, have you had any of the following:

   Abdominal surgery yes no

   If yes, what kind? _____

   Hysterectomy yes no N/A

Appendicitis yes
no

Kidney stones yes
no

The Use of Osteopathic Palpatory Findings in Screening for Nephropathy in Type 2 Diabetes Mellitus: A Pilot Study

Principal Investigator: John Licciardone D.O., M.S., M.B.A
Co-Investigator: Laura Curlee MS4

Recruitment Screening Form - Subject

Subject Identification Number: _____

---

7. In the past month, have you had a urinary tract infection? yes no

8. Have you ever been diagnosed with any of the following:

Conn's syndrome yes no

Addison's disease yes no

Cushing's syndrome yes no

Crohn's disease yes no

Ulcerative colitis yes no

Irritable bowel syndrome yes no

Prostatitis yes no N/A

Benign prostatic hypertrophy yes no N/A

Pelvic inflammatory disease yes no N/A

9. Do you suffer from chronic low back pain? yes no

Name: _____

Phone Number: _____

The Use of Osteopathic Palpatory Findings in Screening for Nephropathy in Type 2 Diabetes Mellitus: A Pilot Study

Principal Investigator: John Licciardone D.O., M.S., M.B.A
Co-Investigator: Laura Curlee MS4

Subject Demographic Information Sheet

Age: _____

Race or Ethnicity:

Black Native American

Hispanic Caucasian

Asian/Pacific Islander Alaskan Native

Gender:

Male Female

The Use of Osteopathic Palpatory Findings in Screening for Nephropathy in Type 2 Diabetes Mellitus: A Pilot Study

Principal Investigator: John Licciardone D.O., M.S., M.B.A
Co-Investigator: Laura Curlee MS4

Pain Documentation Sheet

Pain level: (circle)

0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10

(no pain) (most pain)

The Use of Osteopathic Palpatory Findings in Screening for Nephropathy in Type 2 Diabetes Mellitus: A Pilot Study

Principal Investigator: John Licciardone D.O., M.S., M.B.A
Co-Investigator: Laura Curlee MS4

Palpatory Exam Documentation Sheet

Subject Identification Number: _____

_____

Vital Signs: BP_____ RR _____ Pulse _____

T – Tissue texture changes

Acute Red Reflex (warm, moist, inflamed, red, resilient tissue):

	NONE	MILD	MODERATE	SEVERE
Left	0	1	2	3
Right	0	1	2	3

Chronic Red Reflex: (cold, dry, scaly, itchy,blemished, pale, taut)

	NONE	MILD	MODERATE	SEVERE
Left	0	1	2	3
Right	0	1	2	3

A – Asymmetry

Hypertonicity:

	NONE	MILD	MODERATE	SEVERE
Left	0	1	2	3
Right	0	1	2	3

The Use of Osteopathic Palpatory Findings in Screening for Nephropathy in Type 2 Diabetes Mellitus: A Pilot Study

Principal Investigator: John Licciardone D.O., M.S., M.B.A
Co-Investigator: Laura Curlee MS4

Palpatory Exam Documentation Sheet

Subject Identification Number: _____

_____

R – Restriction of motion: sidebending, rotation, flexion & extension

	NONE	MILD	MODERATE	SEVERE
T10 _____	0	1	2	3
T11 _____	0	1	2	3
T12 _____	0	1	2	3
L1 _____	0	1	2	3
L2 _____	0	1	2	3

T – Tenderness to palpation - circle

T10

Left **0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10**

Right **0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10**

T11

Left **0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10**

Right **0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10**

The Use of Osteopathic Palpatory Findings in Screening for Nephropathy in Type 2 Diabetes Mellitus: A Pilot Study

Principal Investigator: John Licciardone D.O., M.S., M.B.A
Co-Investigator: Laura Curlee MS4

Palpatory Exam Documentation Sheet

Subject Identification Number: _____

T – Tenderness to palpation (continued) - circle

T12

Left **0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10**

Right **0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10**

L1

Left **0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10**

Right **0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10**

L2

Left **0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10**

Right **0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10**

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