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The skeletal pathology slipped capital femoral epiphysis (SCFE) is one of the more common hip diseases that can affect adolescents. Delays in diagnosis and the risk of contralateral SCFE are recognized issues for this patient population. However, SCFE studies often do not include the groups of people most often diagnosed with this pathology, namely Black and Hispanic individuals. This project aimed to address this literature gap by investigating the recognized issues with a sizeable sample of individuals in those ethnic groups, roughly equal to the White patient group. We found that the severity of SCFE measured by Southwick slip angle (SSA) is significantly associated with both insurance type and patient status. Patients who were covered by private insurance or were already an established patient at the medical center were more likely to be diagnosed with mild SCFE, and patients with no insurance had a significantly higher mean SSA than patients with insurance. Posterior sloping angle (PSA) and physeal sloping angle in the anterior-posterior view (PSA-AP) are two of the most often used measurements to estimate contralateral slip risk. They were not predictive of contralateral slip risk in our sample, except for PSA-AP in male patients. When analyzed within each ethnic subgroup, we found significant differences in the PSA and PSA-AP between males and females within the Hispanic patient sample only. This suggests that these angles are not necessarily predictive for all patients groups, and/or that there may

be sex differences within patient populations that can affect the utility of these metrics. To the authors' knowledge, the above findings are the first to link SSA to insurance status and patient status, and to the first to analyze the PSA and PSA-AP angles of a Hispanic SCFE patient group.

DOES DIVERSITY MATTER?

DISPARITIES IN DIAGNOSTIC DELAYS AND CONTRALATERAL RISK FACTORS

WITH SLIPPED CAPITAL FEMORAL EPIPHYSIS

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DOES DIVERSITY MATTER?

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DISSERTATION

Presented to the Graduate Council of the University of North Texas Health Science Center at Fort Worth in Partial Fulfillment of the Requirements for the Degree of

DOCTOR OF PHILOSOPHY

By

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CHAPTER 1

INTRODUCTION

Slipped Capital Femoral Epiphysis (SCFE) is one of the most common hip pathologies in the pediatric population. In this disorder, the physis (growth plate) between the femoral head and neck loses its stability and the femoral head "slips" posteriorly (back) and inferiorly (down) from the femoral neck. This causes pain and hip instability and requires surgery to prevent further morphological deformation. Early diagnosis and treatment are important for the best possible prognosis, unfortunately delayed diagnosis is a recognized problem for this patient population[1–16]. Extant research has identified a handful of possible causes, but the focus has often centered on clinician error rather than barriers to care that patients may experience. But even once a patient with unilateral SCFE has undergone surgery, the risk of the contralateral hip being diagnosed with SCFE later on exists until the physis fuses during skeletal development. Current researchers do not agree on what is best practice for the unilateral SCFE patient or what is a reliable risk factor for a contralateral SCFE, due in part to the varied results and recommendations present in the literature. Both the initial diagnostic delay and the contralateral slip risk represent problems that do not have clear causes or solutions. Early treatment of SCFE patients, as well as an accurate assessment of further slip risk, is beneficial for both patients and surgeons.

SCFE is diagnosed at a significantly higher rate in Black and Hispanic children compared to White children, highlighting the need for more research that includes these ethnic groups

[17–19]. These populations are also more likely to experience health disparities and barriers to care which can delay or prevent treatment for health conditions [20–27]. However, many studies which examine delays in diagnosis for SCFE do not identify the race/ethnicity of their sample and do not examine the variation between and within different ethnicities. Because SCFE is a progressive disease, delaying the treatment of SCFE will likely lead to a moderate or severe slip, and delay increases the likelihood of a poor outcome in overall hip health [1,6,12] [12,28,29]. Examining how barriers to care may affect the SCFE patient population provides a more complete understanding of how delays in diagnosis occur, and hopefully how to improve this variable.

SCFE patients who present unilaterally are also at risk for a contralateral slip. Age, BMI, acute onset, and posterior sloping angle (PSA) have all been indicated as possible contributors to bilateral SCFE, but few articles reach similar conclusions regarding which factors are most indicative of a contralateral slip [30–36]. Only a handful of contralateral slip risk studies have included a sizeable ($n > 12$) sample of Hispanic patients[37–41], and only one mentioned any analysis of race/ethnicity within the study[38]. The pelvis and proximal femur are subject to loading forces, genetics, and sexual dimorphism that affect skeletal morphology. Researchers in the fields of anthropology and orthopedics have observed variations in hip shape within populations and between populations[42–49]. Thus, measuring hip metrics from multiple populations may illuminate possible variations that could confound contralateral slip risk estimations.

For the patient with unilateral presentation of SCFE, surgeons and patients are required to make a decision whether to prophylactically pin the unaffected hip. The lack of clarity over etiology and contralateral slip risk prevents a consensus on what is best practice, with some

researchers arguing that the benefit of contralateral slip prevention outweighs the risks[34,50] , while others maintain that any prophylactic pinning does not benefit the patient long term[51].

Contralateral slip risk factors and the health disparities within the SCFE population are two issues that are still contested and not thoroughly examined. The lack of patient diversity in the research prevents a more complete understanding of these topics; both of which are important in practice. Understanding the socioeconomic factors that can increase the likelihood of SCFE and a poor prognosis can highlight possible barriers to care affecting pediatric health that should be further examined. Identifying statistically significant risk factors for a contralateral slip would enable surgeons to make a more informed decision and lessen the chances of patients undergoing an unnecessary surgery for prophylactic pinning, or conversely developing a contralateral slip.

Skeletal development and hip anatomy

The human hip is a ball and socket joint where the head of the femur articulates with the acetabulum (socket of the hip bone). Both of these bones are formed through endochondral ossification, a process which begins in the prenatal period and continues until skeletal maturity. The process of endochondral ossification that occurs in utero can be divided into four phases. A hyaline cartilage "model" is used as the blueprint for bone formation, and the first phase of this process is the vascularization of the perichondrium (the outermost layer of the hyaline cartilage model). This allows for the mesenchymal cells within the perichondrium to differentiate into osteoblasts, which are cells that deposit osteoid. Second, osteoblasts deposit osteoid along diaphysis (shaft) of cartilage, which forms a bony collar, while the chondrocytes begin to hypertrophy and a calcified matrix begins to form. The calcified bony collar prevents nutrients being delivered to chondrocytes at the center of the hyaline cartilage model, and the subsequent

cell death creates a central cavity (to become the medullary cavity). In the third phase, a periosteal bud consisting of an artery, veins, and nerves forms and invades this cavity, thus allowing osteoblasts and osteoclasts to enter and begin depositing trabecular (spongy) bone matrix. The final stage involves the primary ossification center continuing to ossify until the chondrocytes are concentrated on the ends of the primary ossification center to form the metaphysis area of the long bone. This is where appositional (lengthening) of bone occurs in the area known as the physis (growth plate or epiphyseal plate). Secondary ossification centers of bones generally appear in the post-natal period and are usually located in the epiphyses (ends of long bones that articulate with another bony surface in a joint).

The primary ossification of the femur (diaphysis) forms around 7-8 weeks in utero[52,53]. The secondary ossification center of the femoral head at the proximal (towards the torso) end of the femur which articulates with the acetabulum (the "socket" element of the ball and socket joint of the hip) appears by the end of the first year after birth[52,53]. The other secondary ossification centers of the femur form much later. The lesser trochanter forms around 3 years of age, and the greater trochanter around 2-5 years of age[52], and <2 years of age possibly for females[54]. Both the greater and lesser trochanters are important muscle attachment sites for the gluteal and iliopsoas muscles, but do not affect linear growth[55].

Fusion of these secondary ossification centers to the shaft of the femur differs by area. The femoral head fuses around 12-16 years of age for females, and 14-19 years of age for males[52,54]. The greater trochanter fuses at approximately 14-16 years of age for females, and 16-18 years of age for males [52,54]. The lesser trochanter fuses around age 11-14 for females, and 14-16 for females.

The pelvis consists of the sacrum and right and left hip bones. The hip bones are composed of three primary centers of ossification present at birth: the ilium, ischium, and pubis. The primary ossification center for the ilium appears around 3 months in utero, coinciding with the placement of the sciatic nerve. The ischium primary ossification center emerges around 4-5 month in utero, and the pubis 5-6 months in utero[52,56]. These three bones all form parts of the acetabulum, and before skeletal maturity they are clearly delineated within the acetabulum, thus it is called the triradiate area and is often used in estimating bone age.

The ischium and pubis fuse together first as the ramus around 5 to 8 years of age [52,56]. Fusion of the acetabular region begins at approximately 11 in females and 14 in males and is complete by 15 to 17 years of age[52,56]. The sacrum is part of the spinal column and articulates with the posterior portion of the ilium and the sacro-iliac joint. The sacral primary ossification centers are present at birth and by age 6 all primary centers are fused, with the posterior spinous process joining the bone later between ages 7-15[55].

The formation of the ossification centers, both primary and secondary, as well as the fusion of the physis, varies depending on the bone, sex, and environment. Most females reach skeletal maturity 2-3 years earlier than males, and this is generally attributed to the indirect and direct effects of estrogen on skeletal growth[52,57,58]. Consequently, the final stature for females is achieved by age 17-19, as opposed to 18-20 in males.

The femoral head and neck, like all living structures, are dynamic and respond to external forces. The hip joint is subject to loading conditions with multiple force variables at play including body weight, joint reaction force, and muscle force. Because the axial skeleton is still growing during adolescence, the femur is more adaptive and responsive to changes in the forces applied during this time than after skeletal maturity when most physes have fused and

longitudinal growth ceases. Physical activity and lean mass are often observed to be significant contributors to bone mineral density, and perhaps even morphology, in the proximal femur[59–62]. Nutrition can also affect skeletal growth, and a diet that is deficient in certain nutrients can delay bone development or even induce a pathology such as rickets in the case of Vitamin D deficiency[63–66].

Capital femoral physis growth

The trabecular formation of the proximal femur reflects an adaption of the bone to applied forces, although there are multiple models for how the trabecular bone adapts and compensates for these forces[67]. Pediatric obesity correlates with increased compression and shear forces on the hip joint, and this population does report a greater incidence of hip joint and hip pathologies than their normal weight peers [68]. The growth plate of the proximal femur also responds to increased compressive loading by reducing cell proliferation and growth[69]. Since not all obese children develop SCFE, and there are incidences of normal weight children developing this disease, the increases in shear and compressive forces on the hip must create a different environment in the hip of the SCFE patient versus the non-SCFE patient. This is why the morphology of the hip, specifically some of angle metrics in the growth plate, is one of the foci of research for SCFE.

The highest risk age for SCFE developing is between the ages 11-14, the period 2-3 years before fusion of the physis between the femoral head and neck. This is the period of greatest instability for the physis because of an increase in shear stress. During a child's life until the approximate age of 11, the growth plate is quite rugged, providing a better surface for stability and connectivity[70]. The plate then changes to a more "convex meniscus" and loses its uneven

surface, possibly providing a weaker area that is less resistant to shear forces[70]. The angle of the physis is measured differently by various researchers, but they all aim to examine the vertical inclination of the physis of the femoral head. One of these measurements called the physeal sloping angle taken in the anterior-posterior (PSA-AP) view on a radiograph is associated with both unilateral and contralateral SCFE[71]. It is defined as the angle that forms between the plane of the physis and the horizontal axis of the pelvis in the AP view on a radiograph (Fig 1).

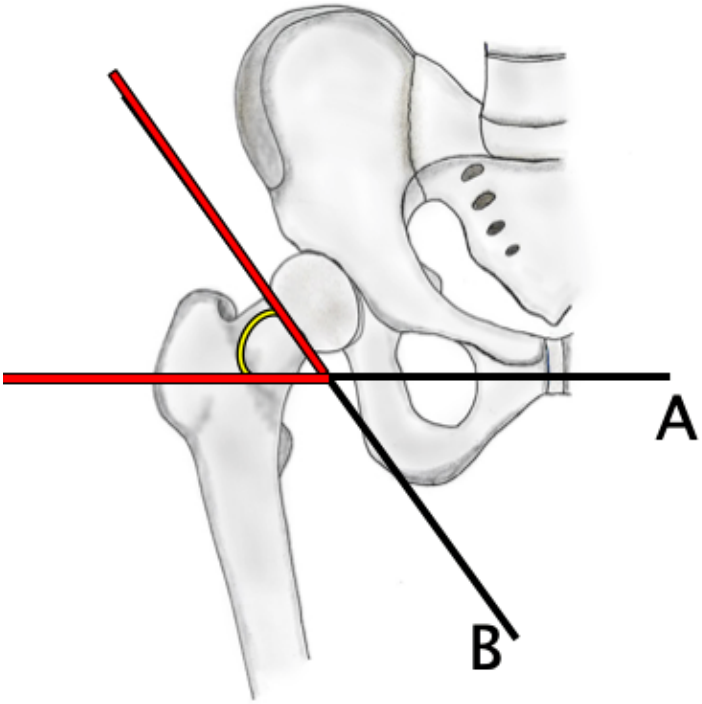

Fig 1: PSA-AP where line A is the horizontal line of the pelvis, and line B is the axis of the physis. The PSA-AP is the angle of lines A and B.

The angle of the capital femoral epiphyseal plate changes from birth and inclines approximately 14 degrees between infancy and the onset of puberty, after which there is little age-related change. However a study by Novais et al. (2018) did observe significant differences between males and females [72–75]. Several studies have noted that the physis inclination in patients would create a higher degree of shear stress, thus possibly contributing to the

development of SCFE. A recent study from Sadeghian et al. (2020) demonstrated through a finite element model that physis on the proximal femur likely grows in a manner that minimizes shear stress on the physis[76]. This natural growth trajectory somehow becomes disrupted as the physis of many SCFE patients trends towards a more vertical PSA-AP, which compromises the stability of the proximal femur[71,77,78]. Zupanc et al. (2008) demonstrated that the increased PSA-AP observed in SCFE patients enabled an increase in shear stress on the proximal epiphysis of the femur[77].

The posterior sloping angle (PSA) is a hip metric that some researchers identify as a reliable indicator of contralateral slip [34,71,79–83]. Similar to the PSA-AP, the PSA is a metric which likely indicates the shear stress placed on the proximal femoral physis. The PSA is the intersection of the plane of the physis and a line perpendicular to the longitudinal neck–diaphyseal axis in the frog leg view (Fig 2). Shearing forces do not just exist in the vertical plane, but also act on the neck to push back in a posterior direction. A larger PSA creates more instability in the joint, decreasing the ability of the physis to withstand stress without deformation[34,71,84]. This is an important component of the overall shearing force that act on the femoral head physis, and thus has been the one of the most researched hip metric for contralateral slip risk so far.

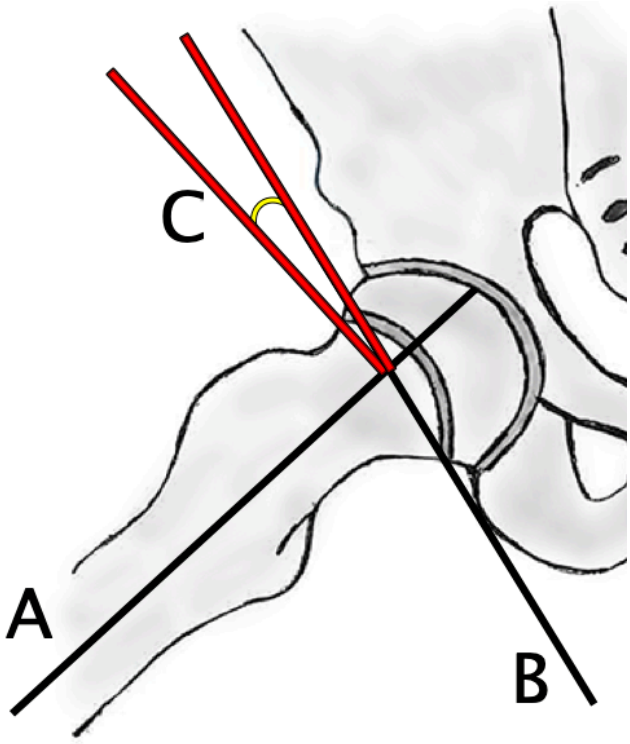

Fig 2: PSA where A is the axis of the femur diaphysis, B is the axis of the physis, and C is the line perpendicular to the diaphyseal line A. The PSA is the formation of the angle of lines C and B.

Risk factors and demographics for SCFE

The risk factors and demographics of the SCFE patient population point to a multifactorial pathogenesis for this disease. Biomechanical, endocrine, and genetic processes have been implicated in SCFE's etiology because of the tendency toward a higher BMI[85,86], male preponderance, an early association with endocrine disorders[87], and a larger proportion of SCFE in certain ethnic groups[18]. The biomechanical factors do not only include obesity, since there are morphological variations in the hip joint that may preclude an individual to SCFE such as PSA [68,78].

While there is a recognized age range of when idiopathic SCFE is most likely to occur, females tend to present younger than males because of earlier skeletal maturation [51,71,86,88]. Interestingly, the general age range for SCFE diagnoses has decreased from 13-15 to 11-13 years

of age in the last several decades, possibly due to the secular trend of earlier pubertal onset in adolescents[17,18,89]. This reduction of age presentation supports the current theory that there is a specific window of time in skeletal maturation that individuals are at the highest risk to develop SCFE [17,18,90]. Atypical SCFE, which is SCFE that presents secondary to another pathology, does not follow this pattern since the comorbid pathologies delay or prematurely accelerate skeletal maturation[17,91,92].

SCFE disproportionately occurs more in certain racial and ethnic groups than others. Hispanic, Black, and Polynesian children develop SCFE more than children in other populations[17,18]. The etiology behind this observation remains unclear; while genetic and morphological causes are possible, no genes or morphological differences between populations have been identified to be consistently associated with a higher risk of SCFE.

A regular observation in idiopathic SCFE patients is the tendency toward obesity or high percentile of weight for age[33,89,90,93]. This was supported with a study in Bronx, New York utilizing appropriate BMI for age indicating that 81% of the SCFE patient population had a BMI in the 95 percentile (obese)[85]. The authors admit, however, that the significance of their findings ($p = <0.001$ when compared with controls) may be limited to their patient group, which was majority Black children.

The importance of weight to the development of this disease may be relevant to the population, since in a Japanese study the percentage of normal weight adolescents with SCFE was 47% and 50.7% for males and females respectively, with even a few underweight adolescents (3.7% for males and 11.9% for females)[92]. Interestingly, Japan had a very low number of SCFE patients until the last 50 years when incidences increased five-fold for males and ten-fold for females in conjunction with overall weight increases for the population[92].

This is also true in Australia, where increases in obesity coincided with increases in SCFE diagnoses[90]. However, the authors noted that aboriginal groups were disproportionately more affected than other populations. These observations support the theory that a higher BMI increases the risk of a child developing SCFE, but also that the parameters for what constitutes a high-risk BMI for this disease may vary by population.

Obesity's contribution to SCFE pathogenesis is often linked to an increase in shear stress placed on the proximal femur. Increased shear forces are tied to epiphyseal instability more so than compressive forces, as shear forces are more likely to displace the epiphysis. This is particularly true when the force is beyond the normal weight of a child[84]. A computerized three-dimensional analysis of shear forces within a SCFE hip revealed an increase in shear force on the proximal epiphysis with an increase in body weight[94]. This model also suggested that the combination of retroversion and excessive weight is enough to compromise the epiphysis. Furthermore, at least one study noted that the incidence of a contralateral slip increases significantly when the patient continued to be obese or became obese post-operatively[33].

Normal weight SCFE patients without comorbidity, however, do exist in the patient population. Additionally, obesity alone does not preclude an individual to this disease (otherwise most obese children would develop SCFE). Other hip mechanic factors found in SCFE patients indicate variations that abnormally increase the strain on the proximal femoral epiphysis.

Treatment

The most common and accepted approach for treatment is single screw in-situ fixation, especially for mild to moderate slips. This surgery carries the lowest risk of complications, however this surgery is most often performed on patients with mild and moderate slips who have

a better outcome in general. The patients with severe slips (Southwick slip angle over 60 degrees) often require an osteotomy of some form, and so other procedures have been developed for severe SCFE patients. Many surgeons will try to improve hip morphology in severe cases because the bone deformation causes damage to the surrounding structures such as the labrum and acetabulum[95,96]. This can occur with mild and moderate slips as well but is more common for severe slips.

Some implants allow for greater growth within the physis, particularly non-threaded cannulated screws[97,98]. However, increased growth of the physis also carried the risk of affixation and a subsequent surgery to re-fix the physis[99]. These devices have recently been favored in the use of prophylactically pinned hips, as it has been shown to reduce the likelihood of coxa breva (short femoral neck with a small femoral head) and coxa vara (the angle between the head and shaft of the femur is reduced to less than 120 degrees) in patients [100].

Health disparities

Delays in medical care can often be attributed to barriers to care within the United States. The variables that can cause an individual to delay receiving treatment are often more pronounced within Black and Hispanic patient cohorts. Because SCFE is more prevalent with these patient groups, knowledge of any impediments to proper care is important. Patients who identify as Black and/or Hispanic are more likely to face adult unemployment, report difficulties in obtaining specialist appointments, be uninsured or under-insured, lack health literacy and access to information, and have a lower household income that White patients[21–23,101–105]. Hispanic individuals can experience unique issues such as language barriers, cultural differences, and immigrant status that can affect health literacy, as well as ease of access to public insurance

options and physician appointments[20,23,25,102,106]. Consequently, Black and Hispanic children are less likely to receive regular medical care and preventative care, and more likely to utilize emergency department services than White children[23,24,107]. Researchers acknowledge that these factors likely have a profound impact on the health of minority children, including higher mortality rates in cancer and more advanced presentation of disease[26,27,108,109].

Orthopedic care is affected by these disparities as well. Medicaid patients have more difficulty in securing appointments with orthopedists for a variety of reasons. First, fewer options for care exist, since public insurance is not accepted at all clinics[15,110–112]. Thus, Medicaid patients often experience a longer time between symptom onset and their appointment[15,103,113]. Second, in many states a referral is required for a patient on Medicaid to see a specialist, which adds more time before a patient can obtain the services they seek [113–115]. These delays can correlate with disease progression, emergency department use, and poorer prognosis with SCFE and other medical conditions.

Slipped capital femoral epiphysis is a progressive disease, and therefore timely care is crucial. Studies that have examined delays in care for SCFE patients have noted an increase in a patient's chances of developing a severe slip the longer the length of time between symptom onset and diagnosis [1,6,14,116,117]. The morphological deformation of the femoral head and acetabulum continues to progress until physeal fusion, and so severe slips often require more invasive and complicated surgeries such as osteotomies to improve the biomechanics of the hip. This creates an additional financial burden on its own in addition to the increased time that parents or a care giver will need to care for the patient [118–120]. A patient with severe slip is in general, apart from any additional surgical procedures, more likely to experience an increased

risk of osteoarthritis, avascular necrosis, hip impingement, and other poor outcomes in relation to pain, mobility, and function [28,29,121–123]. Delays in care for SCFE increase the likelihood of a poor outcome in overall hip health, while early intervention likely means a better outcome for the patient [12,28,29].

Researchers examining delays in diagnosis in SCFE have attributed delays to a few variables. One being vagueness of symptoms, because SCFE can present as knee pain or thigh pain, and so it is sometimes thought to be meniscal tears or muscle strains[6,10,12,14,116,124]. Insurance and socioeconomic status have been correlated with an increased time to presentation, but just a handful of studies have examined this relationship. Only one study had a patient sample that included more than one race/ethnicity, but the Hispanic sample size was only 2 individuals[116]. Kocher et al. (2004) found a clear association between time to initial diagnosis and insurance status, with public insurance holders experiencing greater delays[6]. Hosseinzadeh et al. (2017) found that those without insurance had an increased time interval between symptom onset and diagnosis, but Schur et al. (2016) found no relationship between insurance and diagnostic delays[4,14].

Risk of a contralateral slip

An issue for what constitutes best practice in the orthopedics includes what risk factors contribute to a contralateral slip. The number of SCFE patients that experience a subsequent contralateral slip varies among different studies, with researchers reporting ranges between 12% and 60%[36]. Surgeons have the option of prophylactically pinning the contralateral hip to prevent a possible contralateral slip that may develop later. However, deciding to perform the surgery is largely at the discretion of the physician, because all of the possible risk factors have

varying levels of predictability and few institutions have established protocols. The lack of clarity over etiology and contralateral slip risk prevents a consensus on what is best practice, with some researchers arguing that the benefit of contralateral slip prevention outweighs the risks[34,50], while others maintain that any prophylactic pinning does not benefit the patient long term[51].

A common best practice is to prophylactically pin the contralateral hip if the age of the first SCFE is relatively young, as multiple studies have linked a contralateral slip risk to the age of the first slip[30,125]. However, there is no current consensus of an age "cut off", nor what other factors should constitute a SCFE patient at a high risk for a contralateral slip that justifies a preventative procedure[126]. While most studies indicate that patients with prophylactically pinned hips do not encounter more complications than those who only received treatment on the affected hip, the procedure of a single-screw fixation can affect growth and leg length[127–129]. And the single screw in-situ fixation can cause bone morphology changes on a healthy hip, and so it is not necessarily a beneficial procedure for the patient[38,130,131].

Research into the contralateral slip variables has shown some inconsistent results within different populations and between males and females. PSA is only predictive for females in one study [132], but this difference was not observed in others[34,71]. A recent study by Ou Yang et al. (2021) with an Asian population that included Chinese, Malay, and Indian patients found no predictive power in the PSA for determining a subsequent slip[35]. In fact, the mean PSA (15 degrees) for the univariate group was above many of the proposed risk cut-offs from past studies.

A higher BMI or BMI percentile-for-age at the time of diagnosis for the initial slip has also been seen for contralateral slip patients, but most subsequent studies have not always found this association[37,133]. An increase in BMI after the first SCFE has also been observed as a risk

factor for subsequent slips, but this is not useful clinically in determining which patients might be most at risk for a contralateral slip[134]. While prophylactically pinning is thought to not significantly increase the risk of complications for patients[135], it remains a variable for the patient that may or may not be necessary to add.

Prophylactic pinning

Patients diagnosed with unilateral SCFE face a risk of a contralateral SCFE, and the surgeon treating them may recommend either prophylactic pinning or observation of the unaffected hip until skeletal maturity. The former prevents a contralateral slip but hinders normal growth of an otherwise healthy femur, and the latter allows the hip to grow normally but risks the patient developing a contralateral SCFE later in adolescence. Both options carry risk, including morphological deformation of the proximal femur.

The literature varies on how much risk is involved in a prophylactic pinning procedure, and the complications that are noted usually involve problems such as avascular necrosis and chondrolysis. A few recent studies have examined the morphological changes to the proximal femur as a result of this procedure, with most noting a tendency towards coxa breva and relative coxa vera[99,127,130,131,136–138]. The former can lead to weaker hip abductors as a result of the reduced moment arm of the femoral neck, which may contribute to a gait abnormality that predisposes an individual to osteoarthritis.

While incidents of contralateral slip are mild, even a mild contralateral slip can create a cam-type deformity in the proximal femur [139]. This is defined as a bony prominence in the anterior of the femoral head near the neck that prevent the femoral head from moving smoothly

in the acetabulum. This pathology is associated with femoral acetabular impingement (FAI), and often leads to labral tears and osteoarthritis if left untreated.

As discussed in the previous section, determining contralateral slip risk is not clear-cut. Therefore, the practice of prophylactically pinning the unaffected hip, while it does nearly eliminate the risk of a contralateral slip, is still controversial. The vast majority of orthopedic clinics do not use a uniform set of guidelines to gauge contralateral slip risk, with few exceptions. Therefore it would be of interest to note what trends may exist with patients who undergo prophylactic pinning, and whether any of the identified risk factors appear to factor into this decision. Furthermore, few studies on prophylactic pinning exist in the literature and none of them include data tied to barriers to care which may affect the decision-making of the patients' families.

Specific aims and hypotheses

The current research available on SCFE does not adequately represent the individuals most likely to be diagnosed with this pathology, specifically Black and Hispanic individuals. Moreover, the barriers to care that these populations experience create a higher likelihood of a delayed diagnosis and more severe SCFE. The lack of diversity also prevents a more complete understanding of contralateral slip risk variables because hip morphology varies among populations. Contralateral SCFE, although often mild, may still lead to a cam-type deformity and FAI in the hip. The only preventative solution for contralateral slip is prophylactic pinning, which can also create morphological changes in the hip that predispose it to osteoarthritis. There are sparse studies on patients who have been prophylactically pinned, and what reasoning surgeons use in the decision between observing or prophylactically pinning a SCFE patient. This

project sought to address gaps in the literate on the subjects of health disparities, contralateral slip, and prophylactic pinning in SCFE with a sample population more representative of groups at highest risk for SCFE. To do this, the research design focused on the following three specific aims:

Specific aim #1: Examine how variables associated with barriers to care may affect time to diagnosis and severity in SCFE.

Hypothesis: Most patients diagnosed with SCFE at Cook Children's Medical Center will belong to populations associated with barriers to care. Variables related to barriers to care will be associated with a more severe SCFE diagnosis and a longer time to presentation.

Specific aim #2: Analyze PSA, PSA-AP, BMI, and age for predicting contralateral slip risk and for any variation among race/ethnicities and between sexes.

Hypothesis: PSA and PSA-AP will be significantly different between patients with unilateral vs. contralateral SCFE. Hip morphology will vary among race/ethnicities and/or between sexes.

Specific aim #3: Determine any trends in patients who underwent prophylactic pin surgery.

Hypothesis: Patients with risk factors for contralateral slip will be more likely to receive a prophylactic pinning.

Each following chapter addresses these specific aims respectively. The first chapter is part of a published manuscript, and the second chapter is in preparation for journal submission at

the time this dissertation was completed (November 2022). The third chapter is not currently in preparation for journal submission, but does address the third specific aim. The specific aims of this study and conclusions thereof aim to address these gaps in the hopes of adding to research that may improve health outcomes for patients diagnosed with SCFE.

CHAPTER 2

EXAMINING DELAYS IN DIAGNOSIS OF SLIPPED CAPITAL FEMORAL EPIPHYSIS FROM A HEALTH DISPARITIES PERSPECTIVE

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Introduction

Slipped Capital Femoral Epiphysis (SCFE) is a musculoskeletal condition seen in the pediatric population where the physis (or "growth plate") of the proximal femur between the head and neck becomes unstable, and the femoral head slips posteriorly and inferiorly away from the neck of the femur. Because SCFE progresses until the physis fuses, early diagnosis and treatment is key [1,2,4–7,9,10,12,16,140–143]. Unfortunately, delayed diagnosis with SCFE patients can occur, often in patients with uncharacteristic pain presentation and public insurance. Far fewer studies exist on the latter risk factor, despite several studies indicating that delaying care due to insurance status is associated with a more severe presentation of diseases in general [144–146], The correlation of insurance status with delays in diagnosis is tied to broader issues of health disparities, but this topic has not been well-examined within the SCFE patient population[144,145].

Extant research indicates that patients with public health plans, such as Medicaid, experience more barriers to orthopedic care than those with private insurance, especially regarding delays in treatment [110,147–153]. For example, in many states, patients with Medicaid are required to obtain a referral from a primary care provider before booking an appointment with an orthopedist [148,151,154,155]. Furthermore, doctor's offices are more likely to accept patients with private insurance, and get an appointment sooner, than those with Medicaid. In addition, patients with Medicaid may delay or forgo care due to financial constraints or other barriers [144,156].

Health disparities among racial and ethnic groups are also observed in orthopedic and surgical practices, and often covary with socioeconomic status [153,157–159]. SCFE occurs at a relatively higher frequency among certain populations, in particular Black and Hispanic children,

who are also more likely to receive public health assistance (e.g., Medicaid or Children's Health Insurance Program [CHIP]) than their White and Asian counterparts [17,18,160]. The etiology of the varied incidence rates of SCFE in specific populations is contested within the literature, although larger body size and skeletal morphological variations are common theories [17,19,49,161,162]. Despite Hispanic children being at greater risk to develop SCFE, only a handful of studies include a sizable sample of Hispanic patients as a distinct ethnic group, but these do not examine how health disparities may contribute to diagnostic delays [2,17,37,41,163–165].

The degree of slip severity has been significantly correlated with delays in diagnosis in several studies [1,6,10,12,14,141,142]. A higher slip severity increases the likelihood of premature osteoarthritis and additional surgeries (e.g., osteotomies, and in some cases total hip replacements), whereas a patient diagnosed with a mild slip typically has a better outcome [12,28,29,121,166,167]. Furthermore, a study from Fedorak et al. (2018) showed a direct association between a longer time from symptom onset to diagnosis and a greater chance of more invasive surgery[1]. This study primarily evaluated SCFE within the scope of how health disparities may affect how quickly SCFE is diagnosed and treated. It should be noted that, to the authors' knowledge, this is the first time Hispanic patients have been represented in a study analyzing associations between insurance status and delays in diagnosis for SCFE.

Methods

A retrospective chart review was conducted for patients surgically treated for SCFE at Cook Children's Medical Center (CCMC). This study included patients who underwent surgery from January 2010 to September 2017. Patients diagnosed with SCFE displayed a Southwick

Slip Angle (SSA) of >1°, and other characteristics of SCFE such as widening of the physis. Subjects were required to be 10-16 years of age at the time of SCFE diagnosis and have at least one anatomic study (such as an x-ray) of the affected hip before and after surgery to be included in the study. Patients with comorbidities that precluded an idiopathic SCFE diagnosis, including radiation therapy, endocrine disorders, renal disease, were not included in the study. The Cook Children's Healthcare System Institutional Review Board approved this retrospective study on March 02, 2018, and informed consent was waived per board procedure for expedited retrospective studies.

A total of 133 patients were initially selected that received a SCFE diagnosis within the set time frame, with 4 excluded for being outside the age range, and 5 excluded for comorbidities. This left 124 subjects for analysis. Patient data related to identified SCFE risk factors and health disparity variables were collected, including age at diagnosis, facility of diagnosis, time to diagnosis (in weeks), sex, age, race and ethnicity, height and weight, x-rays to measure slip severity via SSA, and insurance provider. Because of the retrospective nature of the study, not all data points for every subject were available. If the time to diagnosis was given as an estimated period of time (e.g., 3-4 months), a mean of that period would be recorded.

Insurance provider was categorized as private, Medicaid, or none. The facility of the original SCFE diagnosis was gathered from patient notes, but this information was not consistently recorded and therefore not available on all patients. Any visits to medical center of this study prior to the SCFE diagnosis were recorded and noted to be an established patient, as opposed to a new patient, at the time of diagnosis. The non-insurance group was removed for analysis with these two groups, as they are over-represented in the new patient group and may confound results.

The metric of SSA to determine the SCFE grade/severity for each patient was measured by a pediatric orthopedist. It has been established that this measurement has a low degree of intraobserver and interobserver error [83]. The SSA was analyzed as both a categorical variable and continuous variable, as the former is more consistent with previous literature, but the latter provides more information on the spread of variation within the sample. Slip severity was categorized as mild, moderate, and severe. Mild was defined as <30°, Moderate as 31°-60°, and Severe as >61°. BMI-for-age was calculated as a percentile from the CDC website. Race and ethnicity were self-reported from the patient intake form. Thus, "Hispanic" in this study refers to a group of patients who self-identify with the ethnicity and race of Hispanic White. The variable "age at pain onset" was calculated by subtracting the time to diagnosis from the age of diagnosis. Patient data were gathered from files stored in both Athena and Meditech computer programs at the medical center. Data were recorded in the REDcap data capture program, and then exported and analyzed with SPSS 25 once all identifying information was removed. All ratio data underwent testing for normality and homogeneity of variance and with Kurtosis and Levene's test. A $\log_{10}$ or square transformation was used if the data rejected the null hypotheses for normality. Nonparametric tests were used if transformed data did not meet parametric test assumptions.

For normal ratio data, the parametric tests ANOVA, ANCOVA, Pearson's correlation, and linear regression were used. For non-normal ratio data, a Kruskal-Wallis test was utilized. A Tukey's post-hoc test was used for significant ANOVA results. All count data underwent a chi-square analysis, or a Fisher's exact test in the case where at least one cell size was less than 5. Post-hoc tests for count data were conducted using the adjusted residuals and transforming into p-values with a Holm-Bonferroni correction [168].

Results

Black, White, and Hispanic patients were represented with roughly equal sample sizes, with one excluded from analysis because race was not specified (Table 1). The sample included patients of all three categories of SSA severity, with the highest number in the moderate category, with two exclusions because of radiograph quality. The highest frequency of patients were initially diagnosed at the emergency department (41.9%), followed by primary care provider offices (25.8%), and then Orthopedist's offices (17.7%). The mean BMI percentile for all patients was 89.78%.

Table 1: SCFE patient demographics and clinical characteristics summary

Demographic	**n (%)**
Sex	
Male	76 (61.3)
Female	48 (38.7)
Race/Ethnicity	
Black	44 (35.5)
Hispanic	40 (32.3)
White	39 (31.5)
SSA category	
Mild	28 (22.6)
Moderate	69 (55.6)
Severe	24 (19.4)
Insurance Type	
Medicaid	56 (45.5)
None**	9 (7.3)
Private	58 (47.2)
BMI percentile	
Normal weight (5^{th} - 85^{th} percentile)	18 (14.5)
Overweight (86^{th} - 95^{th} percentile)	20 (16.1)
Obese (>95^{th} percentile)	67 (54)

**Eight of the 9 patients in this category filed for Medicaid at time of diagnosis.

The SSA grade was significantly different across the categories of established vs new patients, and insurance types (Table 2). Post-hoc testing revealed significantly fewer established patients presented with a mild SCFE than new patients ($p = 0.01$). Patients with private insurance were more likely to present with a mild SCFE ($p = 0.006$), while patients with no insurance were more likely to present with a severe SCFE ($p = 0.006$). All other chi-square and Fisher's exact testing examining insurance types and patient category, BMI percentile, and race were not significant.

Table 2: Categorical analysis of SCFE severity in patient category and insurance type.

	SSA category			
	mild	moderate	severe	*p-value*
Patient category				
Established, n (%)	13 (38.2)*	15 (64.1)	6 (17.6)	0.046
New, n (%)	15 (17.2)	54 (44.1)	18 (20.7)	
Insurance Type				
Medicaid, n (%)	8 (15.1)	33 (62.3)	12 (22.6)	0.004
None, n (%)	0 (0)	4 (44.4)	5 (55.6)*	
Private, n (%)	20 (23.3)*	31 (53.4)	7 (12.1)	

*Indicates cells with statistically significant difference in post-hoc testing after a Holm-Bonferroni adjustment.

The variables of time to diagnosis, BMI, and BMI percentile underwent log transformations to fit assumptions for parametric testing. Only BMI percentile was still skewed after data transformation, so nonparametric testing was performed for this variable. ANOVAs were run to examine the mean difference in categories within both insurance and race regarding the time to diagnosis, BMI, and SSA (in degrees as a continuous variable). The only significant finding was between groups for insurance type with SSA ($p = 0.003$) (Fig 1). Patients with no insurance had an average SSA of 59.67° (high-range, moderate slip), while patients with Medicaid had an average of 44.7° (mid-range, moderate slip), and private insurance holders had

an average of 38.83° (low-range, moderate slip). A Tukey post-hoc revealed that significant differences exist both between the non-insured and Medicaid groups ($p = 0.044$), and between the non-insured and Private groups ($p = 0.003$), with the non-insured group displaying a significantly higher mean SSA than both the Private and Medicaid groups.

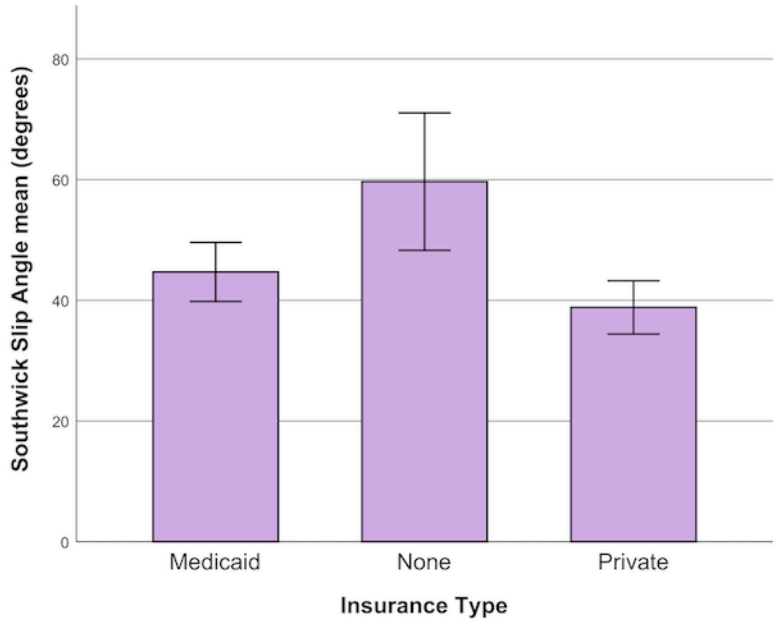

Fig 1. Southwick Slip Angle mean separated by insurance type. Error bars represent 95% confidence interval.

Chi-square analyses revealed significant relationships between insurance type and the facility of diagnosis ($p = 0.017$, Fig 2), as well as between insurance type and race/ethnicity ($p = <0.001$, Fig 3). The emergency department was the only facility where patients with no insurance were diagnosed, but post-hoc testing with a Holm correction did not reveal significant differences between Medicaid and private insurance types. In post-hoc analysis for insurance type and race, significant differences were found with White and Hispanic patients, but not Black patients. Figure 3 shows a significantly greater number of Hispanic patients were on Medicaid (p

= <0.001), while more White patients had private insurance (p = <0.001). Conversely, Hispanic patients were significantly less likely to have private insurance (p = <0.001), and White patients less likely to have Medicaid (p = 0.004).

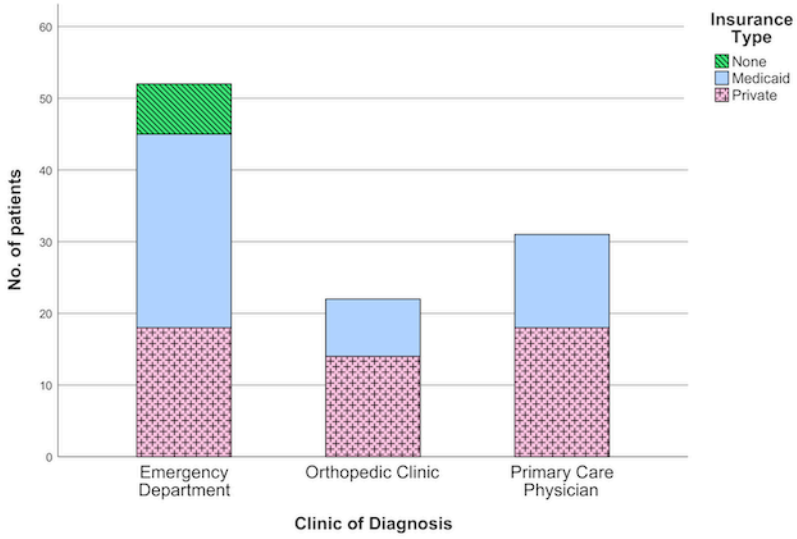

Fig 2. Clinic of diagnosis for patients with each insurance type.

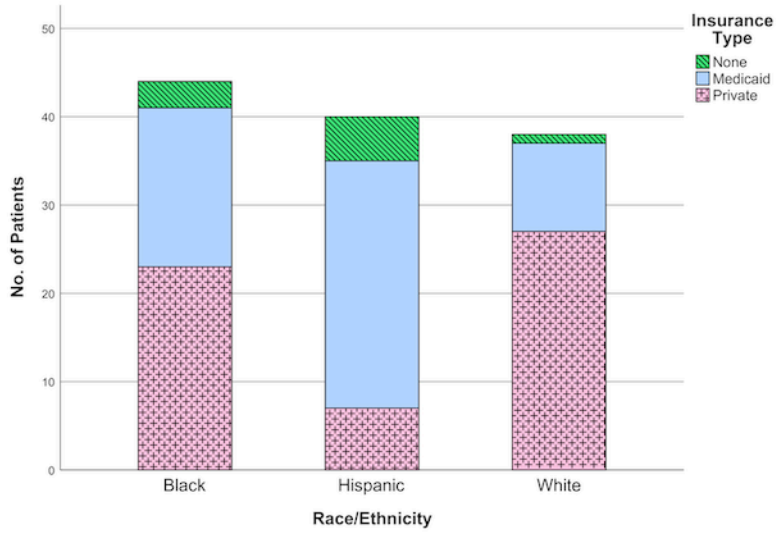

Fig 3. Insurance types separated by race and ethnicity.

Because previous chi-square testing revealed significant differences among insurance types within race/ethnicity groups, an ANCOVA was run to determine if any covariation existed with ethnicity and insurance regarding SSA, BMI, and time to diagnosis. None of the results were significant. Nonparametric testing with BMI percentile and time to diagnosis, insurance type, SSA, and SSA categories yielded no significant results.

A Pearson's correlation matrix revealed significant correlations among BMI, time to diagnosis, and SSA. Multiple linear regression analysis also showed significant associations between time to diagnosis and BMI ($r = 0.347$; $p = <0.001$), and time to diagnosis and SSA ($r = 0.321$; $p = <0.001$).

Discussion

The current study examines what health disparities may exist within the SCFE patient population, and what variables are associated with delays in care and more severe presentations of SCFE. This line of research is also important in evaluating if long-term consequences may exist for patients diagnosed with SCFE who experience barriers to care. To the authors' knowledge, this is the first study to analyze the direct relationship between insurance type and SSA, and only the second to examine delays in diagnosis with an uninsured sample as a distinct group. All patients diagnosed with SCFE require surgery, and how quickly they are able to undergo surgery after symptom onset exerts a direct effect on SCFE severity and hip health outcome [1,6,12,28,142,167,169,170]. The number of Hispanic patients in this sample was also notable and important for inclusion, considering they are at higher risk for SCFE than White patients [17,18,163], and few previous studies have included this ethnic group.

In our study, the non-insurance group had a significantly higher mean SSA than the Medicaid and private groups. Additionally, the categorical analysis of the SSA revealed that patients with private insurance were more likely to present with a mild grade SCFE, and less likely to have a severe SCFE than patients on Medicaid or patients who were not insured. Since delays in diagnosis often progress to a more severe slip, these results suggest that the non-insurance group likely had barriers to care that affected the patients' condition and prognosis, and that patients with private insurance faced fewer barriers to receiving the same treatment. Previous research has noted that access to orthopedic care is often restricted, especially for those on Medicaid [147,148,150]. Additionally, orthopedists currently in practice acknowledge that insurance type and socioeconomic status can be a barrier to care [171]. Texas and many other states require patients on Medicaid to get a referral to see an orthopedist – a barrier that patients with Private insurance may not experience. Medicaid recipients also regularly experience delays in acquiring appointments even after receiving a referral. For example, orthopedic clinics are more likely to take private insurance than Medicaid, and patients on Medicaid may be scheduled for an appointment several weeks later than patients with Private insurance [110,147,154,155].

Although a significant difference in the time to diagnosis was not observed among insurance status groups, the time to diagnosis was not available for all patients. Thus, this may have affected the ability to discern a significant relationship among the three insurance status groups. It should be noted that time to diagnosis was a moderate predictor of SSA and showed a positive linear relationship. This is consistent with previous studies [6,10,12,14,141,142], and our results suggest, therefore, that a patient's slip severity is positively correlated with delays in care.

The correlations among insurance types and SSA in our sample demonstrate how barriers to care may result in a poorer prognosis for SCFE patients without insurance. Currently, Texas has the highest rate of uninsured children in the country (partly due to lack of Medicaid expansion) [160]. Severe SCFE is often tied to multiple complications both in the short-term with a greater chance of a more invasive surgery, and over the long-term with a higher risk of osteoarthritis, avascular necrosis, and poorer hip health scores [28,29,121–123,172]. Therefore, examining data of uninsured SCFE patients is particularly important for this area of the country, and our study provides a unique and needed contribution, as well as directions for future research.

Although previous research has noted unique barriers to care that exist within the Hispanic population (e.g. difficulties with acculturation, immigration status, and language) [23,106,173], no significant differences were found with slip severity among the race and ethnicity categories in our study [173]. Additionally, the ANCOVA analysis revealed that race and ethnicity did not contribute to the differences observed in SSA among insurance types, even though a significantly greater proportion of Hispanic patients were on Medicaid or had no insurance. Our findings suggest that, even though Hispanic patients typically experience unique barriers to care, these factors may dissipate when patients are not underinsured. This aligns with previous studies which attribute a majority of the health disparities observed in Black and Hispanic communities to income and insurance inequality[23,25]. Alternatively, a change in socioeconomic status (from Medicaid to Private insurance) may indicate an overall lessening of these challenges.

The facility of diagnosis can affect the ability to receive proper care, as primary care providers may have trouble identifying SCFE symptoms, especially when presented as knee

pain, and therefore may not believe an immediate referral necessary [2,6,12,141]. Barriers to care may also affect the facility of diagnosis. Previous research has noted that patients insured by Medicaid are more likely to experience transportation difficulties, work schedule conflicts, and barriers obtaining appointments with a primary care or specialist clinic, and thus may choose to go to the emergency department [145,174–177]. Although post-hoc testing did not show a statistically significant difference between the Medicaid and private insurance groups for the clinic of diagnosis in our data, it should be noted that a majority of patients with Medicaid (51.9%) presented at the emergency department for diagnosis. Additionally, the difference in sample size between the uninsured and insured groups may have skewed the post-hoc testing. Interestingly, established patients at the medical center were more likely to present with a mild SCFE than new patients. Our data did not indicate a significant relationship between insurance status or race and the new/established patient groups; therefore, it is possible that established patients insured by Medicaid experienced fewer barriers to care than patients insured by Medicaid who were not established patients. Cook Children's Health Care System (HCS) includes several neighborhood clinics intended to serve as medical homes for patients to receive continuous and preventative care, where the staff speak both English and Spanish. Cook Children's HCS also does routine healthcare outreach to help improve healthcare literacy to lower income groups. The medical home model is patient-centered and focuses on comprehensive, continuous care and accessibility by building relationships between patients and providers. Clinics that follow this model are associated with better healthcare outcomes and adherence with patients reporting fewer barriers to care [178–180][114–116]. The results of this study suggest that outreach efforts such as those utilized by the Cook Children's HCS reduce barriers to care for the Medicaid population. This correlate should be examined with a more

robust sample size and more data before any causal conclusions can be made, especially since a thorough review of the literature did not reveal any studies on delays in SCFE diagnosis that include this variable as a possible correlate to barriers to care.

The linear relationship between BMI and time to diagnosis is noteworthy, and has been reported in only one other study[14]. This correlation suggests that delays in care for SCFE patients may be more complex than previous research has indicated. Current healthcare providers acknowledge that unfavorable views toward obese patients exist, and multiple meta-review studies have indicated these negative perceptions have persisted for many decades in the healthcare field [181–185]. Obese patients have reported feeling dismissed by their healthcare provider regarding pain concerns [181,185,186]. Patients who are obese and encounter weight stigma from their healthcare providers report decreased trust in the health care system, and are more likely to delay or forgo care[187–191]. A higher BMI can correlate with lower socioeconomic status, and result in concerns of treatment cost; however, income information was not available for this sample. The relationship between delays in diagnosis and BMI within the SCFE patient population should be further studied, as this patient population tends to be overweight or obese, and therefore any delays in care regarding this risk factor would be beneficial to address.

Several limitations for this study exist. First, it is a retrospective study, and therefore not every variable was available for each patient because much of the data were self-reported or incomplete (e.g., time to diagnosis and BMI). Second, this is a relatively small study that includes one healthcare system in one state, and thusly may not generalize to other areas of the United States. Third, more nuanced information regarding the private insurance group, such as co-pay, deductible, and organization type, was not available. Therefore, any barriers to care

within the private insurance group, such as high copay and deductible and their effect on SCFE diagnosis, were not observable.

The significant relationship between insurance type and SSA (as both a categorical and continuous variable) shows how being underinsured, and in particular uninsured, may negatively affect a patient with SCFE. The health disparities within the SCFE patient population highlight how barriers to care may impact multiple variables and can compound to affect patient treatment and prognosis. Future research could include interviewing patients about their experiences in obtaining an orthopedic appointment to specify and expand on the barriers that exist for this patient population.

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CHAPTER 3

CONTRALATERAL SLIP RISK IN SLIPPED CAPITAL FEMORAL EPIPHYSIS: THE IMPORTANCE OF POSSIBLE POPULATION AND SEX VARIATION

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Introduction

Any patient with a unilateral presentation of Slipped Capital Femoral Epiphysis (SCFE) is at a higher risk for a contralateral slip than the general population [192]. This pathology can range from mild to severe, with the Southwick Slip Angle (SSA) used most often to assess the severity of the deformity. Clinicians can reduce this risk by prophylactically pinning the unaffected hip on patients who are the most likely to experience a contralateral slip. However, the rates of how often a subsequent slip occurs varies widely in the literature [193]. Furthermore, the studied risk factors for subsequent slips in idiopathic SCFE are not consistently predictive; thus using them for risk assessment is controversial.

Several researchers have examined the posterior sloping angle (PSA) of the physis and the physeal sloping angle in the anterior-posterior view (PSA-AP) to estimate contralateral slip risk, but differences between sexes [80,125], varied cut-off ranges [34,71,80,83,194], and non-significant results[35,79] indicate that this variable may not have a straightforward application to risk assessment. Similarly, researchers have found inconsistent results with other major risk factors such as BMI [31,33,195–197], age [18,198], and Oxford bone score [36,195,199,200]. This lack of clarity in the literature prevents a consensus, with some researchers arguing that the benefit of contralateral slip prevention outweighs the risks[34,50,201], whereas others maintain that any prophylactic pinning does not benefit the patient long term[51,192,202,203].

Certain population groups, such as Black and Hispanic individuals, are at greater risk for SCFE[19,204]. However, these populations are not well-represented in contralateral slip risk research. Many studies do not explicitly identify the race and ethnicity of their patient population, or their patient population is majority or entirely white. The lack of diversity in the literature prevents a complete understanding of how hip morphology may contribute to

subsequent slips, because significant variations in femoral and pelvic metrics among Hispanic, Black, Asian, and White adults have been noted in several studies [45,205–209]. Therefore PSA and other variables may be unreliable when applied to populations not previously studied [35]. Thus, it is important to conduct research with a greater diversity of patients, but few SCFE studies exist that examine sex and ethnicity variations in the context of contralateral risk factors. While a handful of contralateral risk factor research studies have included Hispanic patients in contralateral slip risk analysis[31,39–41,79,193,197,210], only two have an $n > 12$ of Hispanic patients [41,197].

Our study is unique because it is one of the few studies on SCFE to include a relatively equal race/ethnicity distribution that includes Hispanic patients. And to the authors' knowledge, it is only the second study to examine contralateral slip risk variables between ethnicities (the other study being Park et al. 2010), and the first study to do such with a sample that includes a Hispanic population. The purpose of this study is to add to the body of knowledge regarding PSA and PSA-AP metrics within the SCFE population, determine risk factors for contralateral slip for an ethnically diverse sample, and evaluate if there are any variations among the ethnic groups and between sexes.

Methods

A retrospective chart review was conducted for patients surgically treated for SCFE. This study included patients who underwent surgery from January 2010 to September 2017. Patients diagnosed with SCFE displayed a SSA of >1°, and other characteristics of SCFE such as widening of the physis. Patients with initial visits from September 2016 to September 2017 would not be included in contralateral slip analysis to account for the time between initial slip and contralateral slip presentation. Subjects were required to be 10-16 years of age at the time of

SCFE diagnosis to reduce confounding variables such as an undiagnosed endocrinopathy, and have at least one anatomic study (such as an x-ray) of the affected hip before and after surgery to be included in the study. Patients with comorbidities that precluded an idiopathic SCFE diagnosis, including radiation therapy, endocrine disorders, renal disease, were not included in the study. The institutional review board approved this retrospective study on March 02, 2018.

A total of 133 patients were initially selected that received a SCFE diagnosis within the set time frame, with 4 excluded for being outside the age range, 5 and 5 excluded for comorbidities. For the topic of contralateral SCFE we also excluded 5 patients who initially presented with bilateral SCFE. This left 119 subjects for analysis. A total of 15 patients experienced a contralateral slip, meaning they were initially diagnosed with unilateral SCFE and at a later date experienced SCFE on their other hip. Thirty-six patients were excluded from the unilateral group to be used as a comparison to the contralateral slip group for risk analysis: 13 because of prophylactic pinning of the contralateral hip, 5 for bilateral presentation (patients who initially presented with both hips affected by SCFE), and 18 were lost to follow up. This left 71 patients for analysis as a unilateral control cohort to compare with the patients who experienced a contralateral slip who had a follow up time of at least one year.

To examine differences between sexes and within ethnicities regardless of contralateral risk, the entire cohort of 119 patients was analyzed by separating the cohort into subgroups of race and ethnicity. This is particularly important given the lack of representation of Hispanic patients in the literature, and the inconsistency of PSA as a predictive variable when applied to different racial and ethnic groups.

All variables were checked for normality and homogeneity of variance for parametric tests. A nonparametric test was performed if log transformation proved insufficient in

normalizing the data. ANOVA was utilized to examine mean variances between the unilateral sample and the contralateral sample as well as sex and race/ethnicity variances within the sample as a whole. Chi-square and Fisher's exact tests were used for cross-tabulation analysis. A receiver operating characteristic (ROC) was used for any statistically significant risk factors discovered to examine the clinical utility of the variable in predicting a contralateral slip, and determine if there was a possible cut-off point for the PSA and PSA-AP variables. An ROC graph demonstrates the clinical sensitivity and specificity for each cut-off value for a given variable in discriminating between two patient states (typically, "diseased" and "nondiseased")[211]. An ideal ROC graph has a large area under the curve (AUC) value (scaled 0-1) that would imply the variable has both a high degree of sensitivity and specificity when used for diagnosis. In this case, to diagnose a patient who will develop contralateral SCFE. Discriminate function analysis was utilized to determine the classification power of any sex or race/ethnicity differences among the variables.

Hip metric data of the SSA, PSA and PSA-AP was measured by a pediatric orthopedist. The SSA is measured on a radiograph by the difference of the diaphyseal-epiphyseal angles on each hip. The diaphyseal-epiphyseal angle is formed by the line from the anterior point to the posterior point of the physis at the epiphysis intersecting the femoral axis in a frog leg position. The PSA-AP is defined as the angle that forms between the plane of the physis and the horizontal axis of the pelvis in the AP view. The PSA is the intersection of the plane of the physis and a line perpendicular to the longitudinal neck–diaphyseal axis in the frog leg view. Both PSA and PSA-AP were measured on the unaffected hip.

Results

ANOVAs examining the unilateral and contralateral slip cohorts found BMI, PSA, and PSA-AP to be not significant in the sex-combined group analysis (Table 1). Age was significant ($p = 0.003$). When the two groups were separated by sex, males in the unilateral group had a significantly lower PSA-AP than those in the contralateral slip group ($p = 0.03$). Logistic regression revealed a significant ($p = 0.040$) relationship between PSA-AP and the contralateral cohort group. An ROC curve analysis was used to determine the cut-off for this measurement (Figure 1). When using our sample of contralateral slip patients, a cut-off degree of 31.50 would prevent a contralateral slip for 83% of patients, but 36% would receive a prophylactic pinning unnecessarily. The AUC value was 0.755.

Table 1: ANOVA results comparing unilateral control group with contralateral slip patients, including means and standard deviations(±).

	Unilateral SCFE cohort	Contralateral SCFE cohort	*p-value*
Combined			
No. of patients	73	15	
Age	12.939 ±1.316	11.836 ±1.209	**0.003**
BMI	27.412 ±5.954	24.909 ±4.04	0.186
PSA	9.14 ±6.597	11.29 ±6.81	0.273
PSA-AP	26.7 ±8.203	31.14 ±8.681	0.07
Female			
No. of patients	22	9	
Age	12.206 ±1.179	11.409 ±0.738	0.071
BMI	26.221 ±5.873	23.807 ±3.99	0.324
PSA	10.70 ±6.449	10.25 ±8.498	0.880
PSA-AP	24.50 ±7.917	27.88 ±7.912	0.318
Male			
No. of patients	51	6	
Age	13.255 ±1.253	12.468 ±1.553	0.140
BMI	28.020 ±5.974	26.837 ±3.843	0.701
PSA	8.52 ±6.616	12.67 ±3.933	0.14
PSA-AP	27.58 ±8.227	35.50 ±8.191	**0.03**

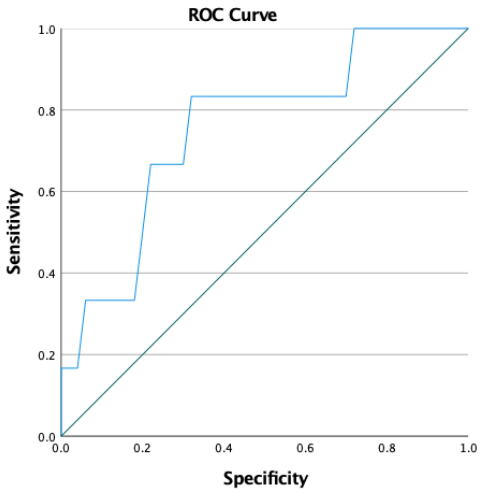

Fig 1: ROC curve for PSA-AP within male unilateral cohort sample in predicting contralateral slip.

A Fisher's exact test found that between the unilateral and contralateral slip cohort; there was no relationship with ethnicity/race, BMI percentile-for-age categories, or insurance status. However, there was a relationship with sex, with a significantly higher number of females than males experiencing a contralateral slip ($p = 0.035$, data not shown).

The variables of BMI, PSA, and PSA-AP were not available for all 119 patients due to inconsistent recording upon intake, and radiographs what did not include the contralateral hip, and the *n* value in Table 2 reflects this fact. Analysis of variables between males and females with race/ethnicity subgroups in the entire cohort group revealed that all three race/ethnicity groups had significant differences in age (Table 2). The Hispanic group also had significant differences between males and females with PSA-AP ($p = 0.001$) (Table 2; Figure 2) and PSA ($p = 0.025$) (Table 2; Figure 3). Discriminant function analysis PSA-AP between Hispanic males and females in the entire cohort indicated that PSA-AP was significant as a classifier variable for

these two groups. Seventy percent of females and 86.8% of males were correctly classified through cross-validation (data not shown).

Table 2: Variables of SCFE patients in entire cohort to examine variations within race/ethnic groups with means and standard deviations.

	Entire Cohort				
	n	Age	BMI	PSA	PSA-AP
Black					
Females	19	11.96 ±1.19	25.23 ± 6.17	9.16 ± 5.7	25.32 ±8.3
Males	21	12.98 ±1.40	28.51 ±7.84	11.0 ±9.42	26.19 ±8.35
p-value		**0.014**	0.153	0.465	0.742
Hispanic					
Females	10	11.55 ±1.10	29.85 ±6.43	17.00 ± 7.27	20.50 ±5.70
Males	28	13.25 ±1.32	27.56 ±4.97	10.61 ±7.5	28.32 ±6.32
p-value		**<0.001**	0.280	**0.025**	**0.001**
White					
Females	13	11.91 ±0.77	25.78 ±5.05	12.08 ± 11.27	29.00 ±9.53
Males	21	13.29 ±1.63	27.01 ±5.52	8.1 ± 8.1	29.81 ±8.72
p-value		**0.006***	0.533	0.068^	0.818

*p-value derived from Kurskal-Wallis test

^p-value of $\log_{10}$ transformed data

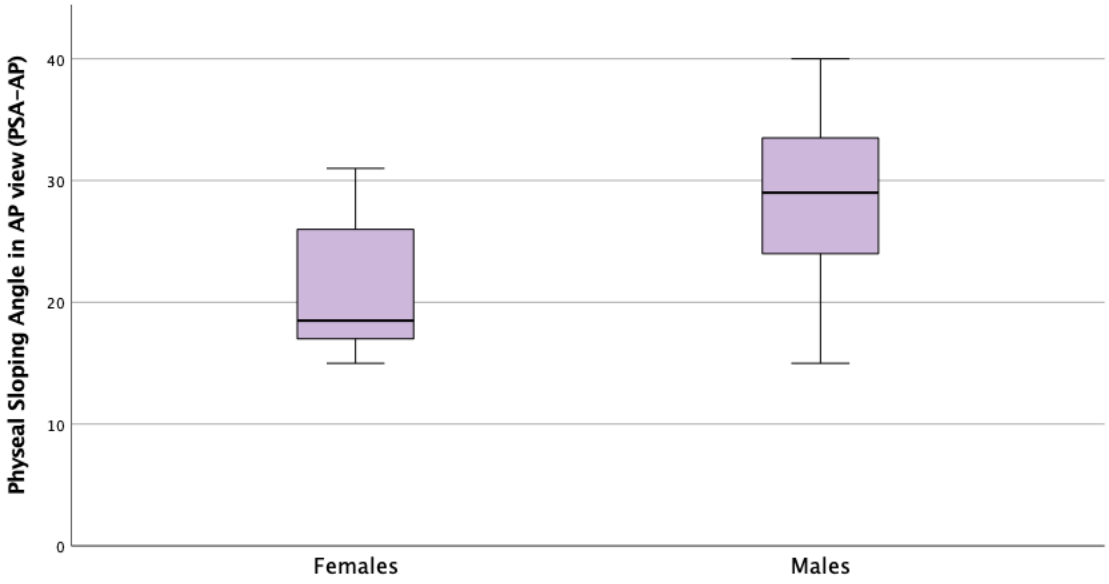

Fig 2: Boxplot of sex differences in PSA-AP within Hispanic patient sample ($p = 0.001$). Horizontal black line represents median and whiskers are the 95% CI.

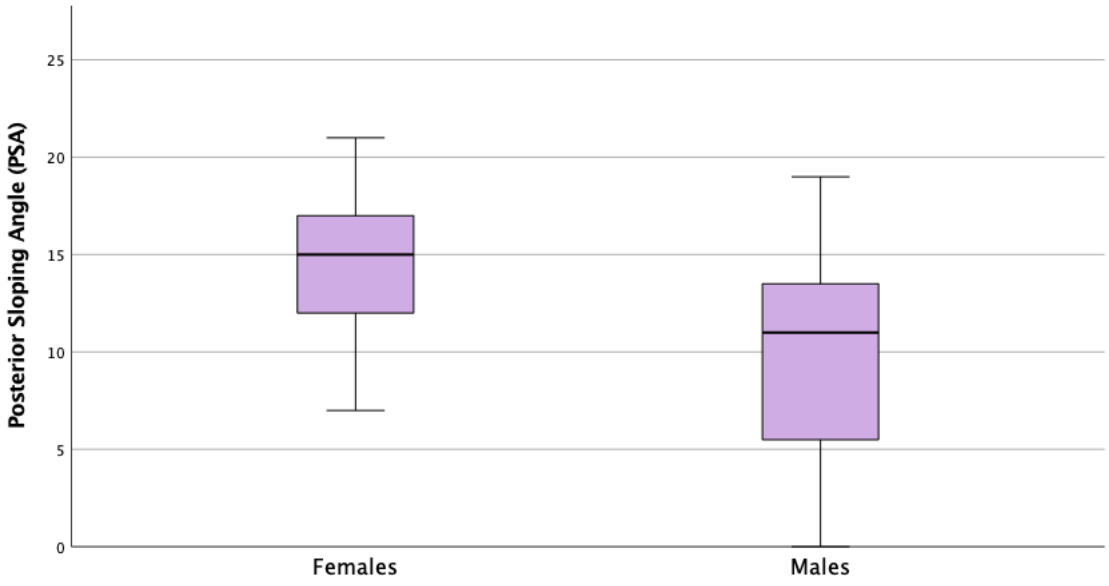

Fig 3: Boxplot of sex differences in PSA within Hispanic patient sample ($p = 0.025$). Horizontal black line represents median and whiskers are the 95% CI.

Discussion

Effectively assessing contralateral slip risk of SCFE patients is an important issue. Prophylactically pinning the unaffected hip significantly reduces the chance of a contralateral slip, but this procedure carries a risk of complications. Ideally, it would prevent any contralateral slips only for patients with clear risk factors for SCFE. Previous studies have examined PSA and PSA-AP in estimating contralateral slip risk, but researchers have reached different conclusions regarding at which point the measurements categorize a patient as high risk "enough" to warrant prophylactic pinning. This is particularly salient with PSA, where the cut-off for patients at high risk for a contralateral slip ranges from 12 to 16 [71,80] and compared to other studies that do not find PSA to be a predictive factor at all [35,199]. In our study, PSA and PSA-AP were not significantly different between the unilateral SCFE cohort and the contralateral SCFE cohort. This suggests that the predictive power of PSA and PSA-AP may not applicable to all patient populations, and should be further investigated.

It is possible that population-based variation is a confounding variable that may explain some of the conflicting information found in studies. Ou Yang et al.[35] recently called into question the utilization of these angles for different races and ethnicities, as their study was the first to examine PSA within an Asian population, and they found no significant differences between the control (unilateral) and contralateral SCFE groups. Despite recorded differences between sexes within and among different populations in the proximal femur [46,205,206,212] and pelvis [44,207,208,213], little is known about possible variation with PSA or PSA-AP regarding sex and race/ethnicity.

Most studies that examine PSA and/or PSA-AP do not state the demographics of their study population [71,214–221]; and those who do often provide no analysis of these variables

between races and ethnicities [38,222,223]. Park et al. [224] analyzed PSA between both sex and race groups of White and African American in their study, but found no differences between them as discrete categories. Similarly, our study found no differences between the Black and White groups. Phillips et al. [225] found no differences in PSA between New Zealand European and Maori groups. However, the period of follow-up time was not controlled for in the unilateral SCFE group, and thus there may have been incidences of contralateral SCFE that were unaccounted for.

The most notable finding in our study is likely the significant difference in PSA and PSA-AP between Hispanic males and females in the entire cohort group. This suggests that cut-off points for certain metric angles may not be applicable equally between males and females of different populations. Furthermore, it implies that the Hispanic group of SCFE patients may have a greater degree of variability between sexes for these measurements, even though the White and Black patient groups did not. This is not unusual in skeletal morphology as the proximal femur, and in particular the neck-shaft angle, varies widely among populations regarding sexual dimorphism [44,46,212,226].

Activity level, lean mass, genetics, nutrition, and a suite of other variables contribute to hip morphology, and thus it is beyond the scope of this paper to speculate on the etiology of the observed differences between Hispanic males and females in our sample. But regardless of the etiology, the data suggest population-level differences in hip morphology that may affect the predictive power of certain metrics. Furthermore, it may be difficult to assess optimal hip morphology without more population-specific information. As several studies have shown that in some populations, even slight morphological variations can lead to osteoarthritis [227], while in others morphological features are only suboptimal when combined together [228]. At the

cellular and genetic level, chondrocytes may be less resistant to hip deformations for individuals who develop osteoarthritis [229].

The ROC analysis did reveal a mildly predictive cut-off point for males in our sample regarding PSA-AP. However, the authors would urge caution when applying this to a clinical setting. As demonstrated in this paper, population variation exists within hip metrics to a degree that may negate the predictive power of this measurement.

Limitations of this study include those normally found in a retrospective study, including that not all patients had BMI recorded, and possible selection bias for the control/unilateral cohort since not all patients followed up beyond one year post-op. There were also not enough patients who developed contralateral SCFE to analyze risk factors within each ethnicity between the control and contralateral groups. Although the PSA and PSA-AP measurements for the Hispanic patients who did develop a contralateral slip were less than one standard deviation from the mean (data not shown), a larger sample of Hispanic patients would be needed to determine if these measurements could be a risk factor with difference parameters for males and females.

CHAPTER 4

TRENDS IN PATIENTS WITH SLIPPED CAPITAL FFEMORAL EPIPHYSIS WHO UNDERGO PROPHYLACTIC PINNING

Introduction

For patients diagnosed with unilateral slipped capital femoral epiphysis (SCFE), managing the risk of a contralateral slip can take two directions. Prophylactically pinning the healthy hip greatly reduces the likelihood of a contralateral slip, but researchers' conclusions differ regarding when and if to employ this practice. Many argue that observation and careful follow-up are sufficient, and that the risks of prophylactic fixation outweigh the benefits[192,230,231]. Others counter that reported complications with prophylactic pinning are mild and infrequent, and lead to less morphological abnormality than if the patient caught a contralateral slip early[99,169,193,232].

Further complicating matters is that while many authors assert that prophylactic pinning should be utilized for patients at higher risk for a contralateral slip, the etiology of SCFE is unclear, and therefore risk factors for subsequent slips are not reliably predictive. Most research studies conclude that patients with atypical SCFE, such as those with endocrinopathies and previous radiation therapy, would benefit from prophylactic pinning[192]. But determining who is most at risk in the cases of idiopathic SCFE is still debated in the literature, and follow-up studies on prophylactically pinned hips are uncommon.

Additionally, it can be difficult to compare studies because they vary greatly not only in average follow-up time, but surgical equipment and techniques. The medical devices to stabilize the hip may restrict or allow continued growth of the physis, and there are trade-offs for each option. Traditionally, a cannulated (threaded) screw has been preferred, which prevents growth but does not stop it completely[130,166,203,233]. More modern techniques involve K-wire, Hanson hook pins, and others that are designed to allow continued growth in the physis [100,233,234]. The former often leads to more marked morphological deformities of the femur,

possibly predisposing the patient to osteoarthritis later in life [127,130,131,233,235]. The latter usually results in a more normal morphology, but the more a patient grows, the more likely they may need the hardware removed or replaced [127,203,236].

Patient adherence to regular follow-ups ensures that clinicians can catch and treat contralateral slips early. Therefore, examining variables between patients who were or were not seen beyond a year may illuminate possible disparities and improve outcomes. Although insurance status can affect health care access, no studies to date have examined how insurance may affect the frequency and duration of follow-up time by patients with SCFE. Differences between patients with a prophylactic pin and those without may also offer a snapshot of the clinicians' judgments regarding who may be at high risk for a contralateral slip. Thus giving possible insights into any "intuitive" leanings or how surgeons are utilizing the available (and conflicting) research on prophylactic pinning. The purpose of this study was to examine how possible risk factors for contralateral SCFE and socioeconomic factors may interplay into the decision to prophylactically pin or observe patients diagnosed with unilateral SCFE.

Methods

A retrospective chart review was conducted for patients surgically treated for SCFE. This study included patients who underwent surgery from January 2010 to September 2017. Patients diagnosed with SCFE displayed a Southwick Slip Angle (SSA) of >1°, and other characteristics of SCFE such as widening of the physis. Subjects were required to be 10-16 years of age at the time of SCFE diagnosis to reduce confounding variables such as an undiagnosed endocrinopathy, and have at least one anatomic study (such as an x-ray) of the affected hip before and after surgery to be included in the study. Patients with comorbidities that precluded an

idiopathic SCFE diagnosis, including radiation therapy, endocrine disorders, renal disease, were not included in the study. The institutional review board approved this retrospective study on March 02, 2018.

A total of 133 patients were initially selected that received a SCFE diagnosis within the set time frame, with 4 excluded for being outside the age range, 5 excluded for comorbidities. Eighteen SCFE patients underwent pinning of both hips; 5 because of bilateral SCFE, and 13 as a precautionary measure (prophylactic pinning). Patients who did not have both hips pinned at the initial diagnosis were categorized as the "observed cohort" because the diagnosis of any contralateral slip was dependent on follow-up visits and subsequent x-rays. To determine if any trends existed among the patients who were prophylactically pinned, they were compared to the group of unilaterally pinned SCFE patients. This anaylsis would serve to uncover what variables (if any) may have contributed to the decision to prophylactically pin one set of patients and not another.

Demographic data included age, sex, race and ethnicity, and BMI percentile-for-age. Hip metric data included SSA to determine slip severity, as well as Posterior Sloping Angle (PSA) and Physeal Sloping Angle taken in the Anterior-Posterior view (PSA-AP). SSA is measured on a radiograph by the difference of the diaphyseal-epiphyseal angles on each hip. The diaphyseal-epiphyseal angle is formed by the line from the anterior point to the posterior point of the physis between the femoral head and neck, at the epiphysis intersecting the femoral axis in a frog leg position. The PSA-AP is defined as the angle that forms between the plane of the physis and the horizontal axis of the pelvis in the AP view. The PSA is the intersection of the plane of the physis and a line perpendicular to the longitudinal neck–diaphyseal axis in the frog leg view.

Follow-up time was calculated as a categorical variable if the patient was seen beyond the 1-year mark, even if there was a significant gap in time between appointments. This is of concern to clinicians who hope that even if patients do not attend regular follow-ups, they will schedule an appointment if contralateral slip symptoms present. Insurance, BMI, sex, and ethnicity were examined in a Chi-square analysis (or a Fisher's exact test when appropriate) to determine variables that may have contributed to the decision to prophylactically pin the unaffected hip. Bloodwork taken within 1 year of the SCFE diagnosis was also included for analysis, focusing on the relevant skeletal health variables of sodium, calcium, Thyroid Stimulating Hormone (TSH), potassium, and Vitamin D.

Results

ANOVA results revealed that the prophylactically pinned cohort and the observed patient cohort did not differ significantly in SSA, PSA, PSA-AP, time to presentation, or duration of care. There was a significant difference with age at diagnosis ($p = 0.001$) (Table 1), but was not significant with females within separated sex subgroups. Established patients who were prophylactically pinned had a higher mean duration of care, whereas the reverse was true for new patients. However, this difference was not significant.

The BMI percentile for age was significantly different between these groups ($p = 0.03$), with all the prophylactically pinned patients in the >95 percentile of BMI for age (Table 2). Patients seen beyond one year did not differ among insurance status or race with pooled subgroups. Only Black patients with Medicaid were significantly more likely ($p = 0.005$) to be seen beyond a year than private insurance patients (Table 3).

Relevant bloodwork was found for 12 patients. Nine had a panel which included Potassium, Calcium, Sodium, and TSH. Potassium, Calcium, and Sodium were normal for all 9

patients, while 3 of the 9 patients had a TSH level measured by mIU/L >4.00, and 2 of those 3 had their contralateral hip prophylactically pinned (Figure 1). Four had a Vitamin D level measured as 25-hydroxy nanomoles/liter (nmol/L) recorded (Figure 2). Three of those 4 had a Vitamin D level <30.

Table 1: ANOVA results of contralateral slip risk variables of observed versus prophylactically pinned cohorts.

	Observed cohort	**Prophylactically pinned cohort**	*p-value*
Combined			
Age	12.84 ± 1.42	11.32 ± 0.75	**0.001***
PSA	9.83 ± 7.07	10.90 ± 10.53	0.470
PSA-AP	26.06 ± 8.52	27.70 ± 7.36	0.716
SSA	42.53 ± 18.06	44.38 ± 17.50	0.82
Female			
Age	11.99 ± 1.08	11.39 ± 0.79	0.193
PSA	10.70 ±6.449	10.25 ±8.498	0.342
PSA-AP	24.50 ±7.917	27.88 ±7.912	0.402
SSA	43.98 ± 18.91	46.86 ± 21.61	0.717
Male			
Age	13.40 ± 1.35	11.24 ± 0.75	**<0.001**
PSA	9.32 ± 7.27	14.75 ± 7.271	0.094
PSA-AP	28.31 ± 8.25	27.50 ± 5.80	*0.851*
SSA	41.74 ± 17.65	41.50 ± 12.47	*0.952*

*p-value derived from log-transformed data

Table 2: Fisher's Exact table of the number of patients in each BMI category for observed and prophylactically pinned groups and results

BMI Percentile	**Observed cohort**	**Prophylactically pinned cohort**	*p-value*
<85th percentile	17	0	0.035
85th to < 95th percentile	20	0	
> 95th percentile	54	11	

Table 3: Fisher's Exact table of insurance type and follow-up times for Black patients and results.

Insurance type	**Seen beyond 1 year?**		
	No	**Yes**	*p-value*
Medicaid	4	17	0.005
Private	14	9	

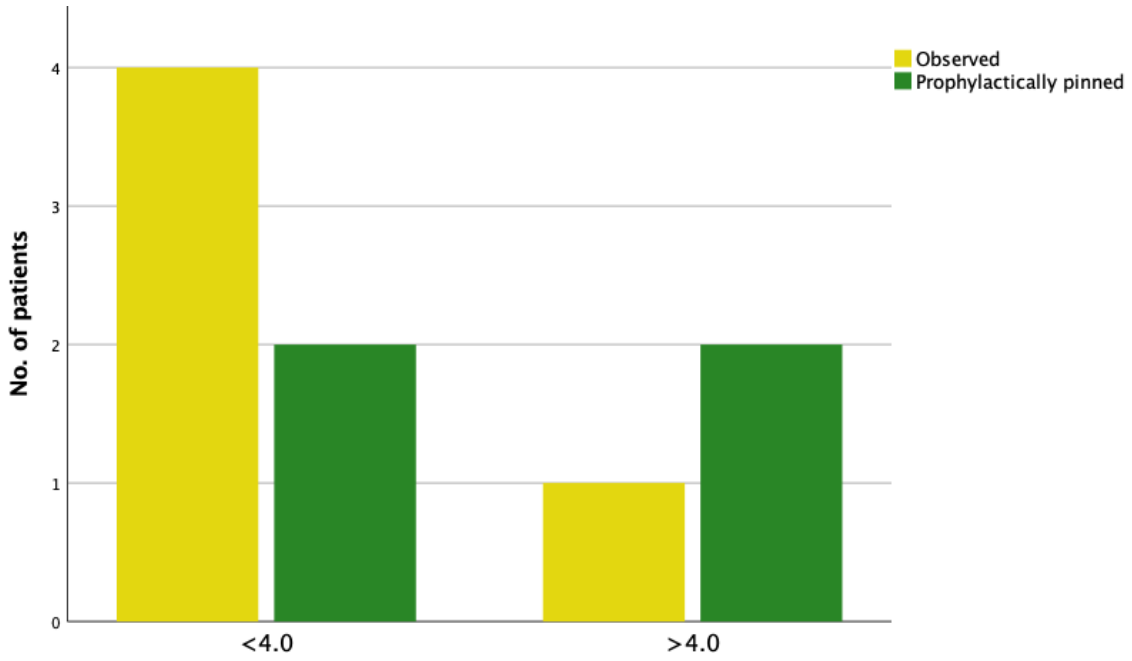

Fig 1: TSH levels by mIU/L for unilateral SCFE patients

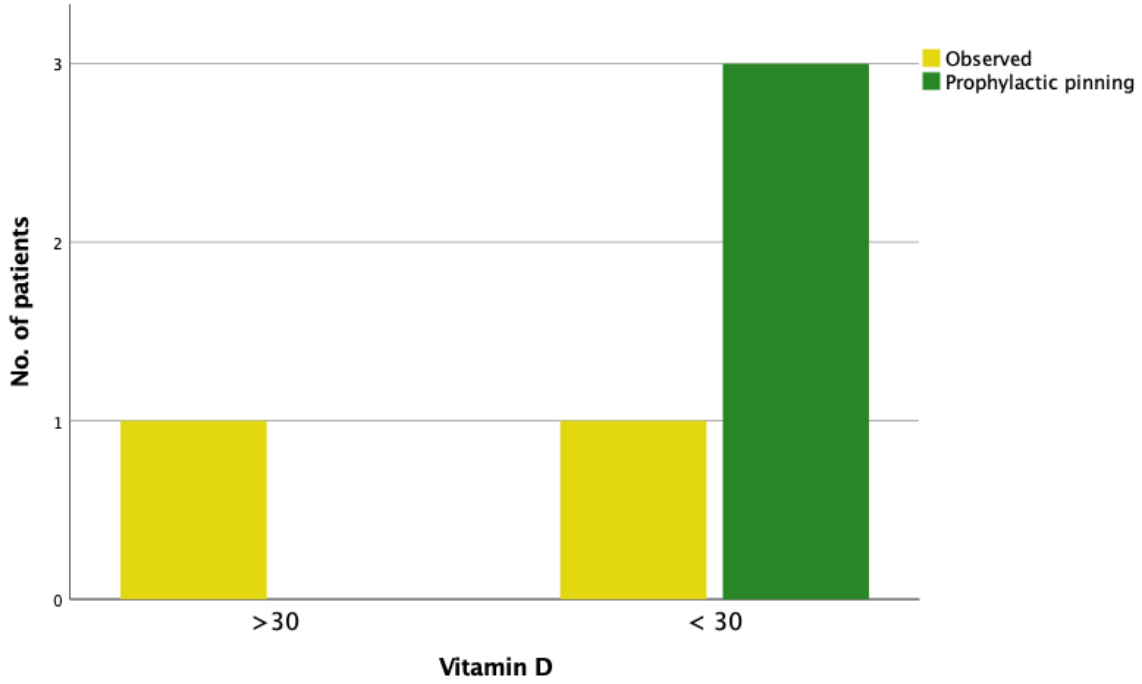

Fig 2: Vitamin D levels for unilateral SCFE patients measured as 25-hydroxy in nanomoles/liter (nmol/L)

Discussion

Unsurprisingly, the prophylactically pinned group was significantly younger than the observed group. This follows the standard of practice that suggests a greater length of time in skeletal immaturity increases the likelihood of SCFE, and allows for possibly undiagnosed endocrinopathy issues. When separated by subgroups, however, only males maintained a statistically significant difference. This may be due to the fact that, generally, males are diagnosed at a younger age than females, but the males in our prophylactically pinned cohort had a mean age closer to that of the females in either cohort.

Hypothyroidism is a recognized risk factor for SCFE as well as contralateral SCFE, however a TSH > 4.0 does not necessarily lead to a clinical diagnosis of hypothyroidism[237–239]. In our study, the patients had a TSH level between 4.0 and 5.58, which is within the normal range for that age group, although it is at the high end and may represent a subclinical hypothyroidism. They were also not formally diagnosed with hypothyroidism at the time of their SCFE diagnosis. It's unclear if the higher TSH levels influenced the decision for prophylactic pinning, but the result indicate the possibility that either the clinician or the patient considered this factor.

Patients diagnosed with SCFE are sometimes identified as having subclinical rickets or low blood serum levels of Vitamin D, but these trends are not consistent [165,240,241]. In this study it's unknown if this factor affected the decision to perform the prophylactic pinning. However, it may point to either the patient or the provider considering these variables. Interestingly, the Medicaid group had more patients who followed up beyond one year than private insurance patients, but only for Black patients. It's unclear why this relationship may exist, as further information regarding income and specific on private insurance costs such as co-pay and deductibles for each patient was not available. This may be a spurious relationship, but further research would be needed to determine if it holds merit.

CHAPTER 5

CONCLUSION

The importance of diversity within the sample patient population for medical research has garnered more attention within the last decade. What is deemed within the normal range, and what may be pathological, can differ between males and females, and among different races and ethnicities[48,242]. Thus resulting in an incomplete understanding of the topic and possibly missing important variables in the underrepresented patient population [243–245].

The absence of more diverse patient population samples in SCFE research creates holes in multiple topics. Studies on delays in diagnosis that do not include patient populations more likely to experience delays in their health care miss an important aspect of this issue. The data presented in this dissertation underscore the impact that barriers to care may have on SCFE severity, as patients who were self-pay at the time of diagnosis had a significantly more severe diagnosis of their affected hip. Patients who were already established patients in the Cook Children's Health Care System were more likely to present with a mild category of SCFE. Furthermore, the number of patients insured by Medicaid versus private insurance did not differ significantly between the new and established patient groups. This may be due to the efforts of the Cook Children's Healthcare System to engage in community outreach and reduce the barriers to care often seen in this area. For example, the neighborhood clinics are employed with staff who speak both English and Spanish. The greater likelihood for established patients to receive a

mild SCFE diagnosis regardless of insurance status highlights how the healthcare field can help patients to overcome possible barriers to care through outreach and community involvement.

One unexpected finding was the positive correlation between obesity and time to diagnosis, which has been reported in only one other study[246]. Patients who are overweight or obese often describe negative experiences with health care providers. Specifically, feeling judged or having their health concerns dismissed. This often leads to a disengagement with the healthcare system and delayed care. Because many children diagnosed with SCFE are overweight or obese, the relationship between perceived weight stigma and delays in diagnosis is worth investing further in future studies.

The contralateral slip risk factors of PSA and PSA-AP have been researched in an effort to determine which patients may be at highest risk for a contralateral slip for patients diagnosed with SCFE. Although some studies have reported a high predictive value for these measurements, this is not consistent throughout the literature. Our study did not find PSA and PSA-AP to be predictive when comparing the unilateral cohort to the contralateral cohort. When the cohorts were broken into subgroups by sex, PSA-AP was mildly predictive for male patients. However, this result did not rise to clinical relevance and should be interpreted with caution.

The Hispanic patient group within the entire cohort had sexual dimorphism with both PSA and PSA-AP, although there was greater significance with PSA-AP. This finding underscores the need to include a greater diversity of racial and ethnic groups within studies examining contralateral slip risk factors. Within the pediatric orthopedic field, and specifically SCFE, several researchers have noted morphological differences for multiple key measurements. Ou Yang et al. (2020) noted that the normal range for PSA in their Asian cohort would be considered high risk according to studies with mainly White American patients. The LCEA,

alpha angle, femoral and acetabular version, and femoral offset have all shown some degree of variability between sexes and/or races in healthy and pathological patient populations. Individuals with similar morphologies in the hip can have different outcomes regarding the development of osteoarthritis, thus suggesting that genetic factors may influence chondrocytes in articular cartilage[229]. Therefore, it may be inadvisable to apply parameters based on one race/ethnicity to the entire patient population diagnosed with SCFE.

The variables of patients who underwent prophylactic pinning of the contralateral hip had a few trends worth noting. First, all of these patients were in the >95 percentile for weight, which was significantly different than the general distribution of SCFE patients. Second, 3 of the 9 patients who had TSH levels measured recently were on the higher end of average and 2 of those patients were prophylactically pinned. While no relationship between insurance type and prophylactic pinning was discovered, out-of-pocket expenses for the privately insured may be a confounding variable.

Several limitations exist for this research. First, not all variables could be collected for each patient, such as BMI and time to diagnosis. Thus, it cannot be known how the missing data may have affected the results of the studies. Second, more detailed information on the private insurance for the patients was not available, so variables such as copay, deductible, and premium that may have affected decisions to seek care and follow up care could not be calculated. Third, not all patients followed up beyond a year, and thus the unilateral SCFE cohort was smaller than it could have been if follow ups on all patients were available.

Future directions for research would expand upon the findings discussed above by including a larger group of patients from each ethnic group. Additionally, more morphological variables should be measured, particularly those that have been shown to differ among other

populations. Researching possible genetic factors that may contribute the development of SCFE would also be beneficial while investigating the morphology, since it may point to differences in chondrocyte resistance to shear stress. Hormonal and nutritional variables may also be a valid line of inquiry, as both are known to affect skeletal growth, and leptin in particular may preclude some children to SCFE[247].

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