Study Protocol

Title: Quality of life following interpolated flap repair of post-Mohs surgical defects of the nose: a multi-center prospective observational cohort study

Short Title: Flaps SCI

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TABLE OF CONTENTS

Abbreviations

MMS – Mohs micrographic surgery

SCI – Skin Cancer Index

QOL – quality of life

Abstract

Context: Address the limited knowledge regarding patient well-being and quality of life (QOL) after interpolated flap repair of post-Mohs surgical defects on the nose.

Objectives: Evaluate QOL after Mohs micrographic surgery (MMS) resection and interpolated flap reconstruction.

Design: Multi-center prospective survey study using the Skin Cancer Index (SCI), a disease-specific, validated questionnaire.

Setting: Academic and private outpatient MMS centers across the U.S. (Goal: ≥5 participating centers)

Participants: Consenting adults ≥18 years old who undergo MMS of a nasal skin cancer with subsequent interpolated flap repair of the defect.

Main outcomes and measures: The primary outcome will be skin cancer specific QOL queried with the SCI at the following time points: pre-operatively, 1 week after flap placement, 4 weeks after flap takedown, and 16 weeks after flap takedown.

1 Background Information and Rationale

1.1 Introduction

Previous research has shown improved QOL after MMS in the outpatient setting. However, the literature is limited to single-center studies and do not explore if improved QOL applies to MMS patients who also have complex reconstruction.

1.2 Relevant Literature and Data

Receiving a skin cancer diagnosis is stressful [1] and skin cancer surgery with subsequent scarring and changes in appearance can also decrease quality of life [2]. Patient satisfaction with skin cancer surgery is associated with the final cosmetic result of the surgery [3] and results interpreted as minimal scarring by a physician may still cause significant anxiety and self-consciousness to the patient [4]. One study found that in order to avoid disfigurement, the majority of adults surveyed would go to any lengths to minimize scarring, even if they resulted in only small improvements in scar appearance [5]. Perioperative use of patient reported outcomes tools such as the skin cancer index (SCI) may help practitioners identify patients with concerns about scarring and offer appropriate support if needed [6]. To date, no studies have systematically evaluated quality of life following interpolated flap repair in the outpatient setting.

1.3 Compliance Statement

This study will be conducted in full accordance of all applicable institution's research policies and procedures as defined by their IRBs. All episodes of non-compliance will be documented.

The investigators will perform the study in accordance with this protocol, will obtain consent and assent, and will report unanticipated problems involving risks to subjects or others in accordance with the Hospital of the University of Pennsylvania's IRB Policies and Procedures and all federal requirements. Collection, recording, and reporting of data will be accurate and will ensure the privacy, health, and welfare of research subjects during and after the study.

2 Study Objectives

The purpose of this study is to determine skin-cancer specific QOL after MMS with interpolated flap repair of nasal defects.

2.1 Primary Objective

The primary objective of this study is to determine the mean difference in overall SCI scores between pre-MMS and 16 weeks after flap takedown. The study will be powered to detect a change of 5% from pre-MMS SCI, based upon an SCI validation study that previously reported a pre-MMS score of 60 and standard deviation of 12.8 [7].

3 Investigational Plan

3.1 Study Population

Patients age 18 years or greater who are capable of providing informed consent and who may require an interpolated flap repair of their post-Mohs surgical defect will be recruited. If they consent to the study, they will be asked to complete the SCI preoperatively. Patients who subsequently undergo interpolated flap repair will be followed. Patients who do not

undergo interpolated flap will not be followed, and their informed consent form and pre-operative surveys will be destroyed in accordance with HIPAA regulations. They will be asked to complete an SCI at 1 week after flap placement, 4 weeks after flap takedown, and 16 weeks after flap takedown. The target enrollment will be approximately 170 patients undergoing interpolated flap repair, in anticipation of loss of follow up. However, this may be adjusted during the study as the percentage of loss to follow-up becomes apparent. A final sample size of 145 is needed to achieve 80% power to detect a mean of paired differences of 3.0, with an estimated standard deviation of differences of 12.8, with a significance level (alpha) of 0.05, using a two-tailed paired t-test between pre-MMS SCI and week 16 after flap takedown SCI scores.

Inclusion Criteria

- Males or females age 18-100
- Diagnosis of a nasal skin cancer
- Undergoing MMS under local anesthesia in the outpatient setting
- Receiving a 2-stage interpolated flap repair

Exclusion Criteria

- Males or females ≤18 years old
- Patients undergoing MMS and repair under general anesthesia in the operating room
- Receiving a nasal defect repair that is not a 2-stage interpolated flap

3.2 Study Design

This will be a multicenter, prospective, observational, cohort study. Covariates collected for all cases will be use of sterile gloves during MMS/reconstruction, type of sterile preparation used, use of antibiotic prophylaxis, use of a hemostatic dressing or agent to the flap pedicle, number of stages of Mohs surgery, same day versus delayed repair, interpolated flap type, whether or not the defect was enlarged to conform to a cosmetic subunit, postoperative defect length and width, and pedicle width for interpolated flaps. Patient demographic and clinical covariates to be collected will include sex, age, anatomic location of the tumor, histologic type of the tumor, immunosuppression, anticoagulant use, tobacco use, and history of diabetes mellitus. Data will be recorded and imported into an online database (RedCap). Data collection will start preoperatively, with subsequent collections one week from the date of the interpolated flap placement, 4 weeks after flap takedown, and 16 weeks after flap takedown. Quality of life (QOL) will be assessed via a skin cancer specific QOL instrument, the skin cancer index (SCI). All data will be stored via a secure RedCap database. For collection of patient SCI scores, patients will complete a structured survey online. If patients do not complete the online questionnaire, they will be contacted via telephone for collection of this data. All telephone interviews for collection of patient SCI scores will occur via a structured interview questionnaire by a trained clinical research fellow.

3.3 Study Duration

The target enrollment goal will be for a total of 170 patients collected over a 2-year period. Time for enrollment is dependent upon the number of Mohs surgeons recruited, and the number of eligible interpolated flaps conducted by each. Active patient participation will last from day of

repair to final SCI, which will range from 18-20 weeks depending on how long the flap is inset prior to takedown. Total study duration is expected to be 3 years to complete enrollment, follow-up, data entry and analysis, and manuscript preparation. The proposed start date is June 1, 2018.

3.4 Subject Completion/Withdraw

Subjects may withdraw from the study at any time without prejudice to their care. The investigator may also withdraw subjects who violate the study plan, or to protect the subject for reasons of safety or for administrative reasons. It will be documented whether or not each subject completes the study. Study completion will occur when/if patient fills out 16-week after flap takedown survey. The patient will be informed that their completion in the study is over at that time and thanked for their participation. If the investigator becomes aware of any serious, related adverse events after the subject completes or withdraws from the study, they will be recorded in the source documents.

4 Statistical Methods

4.1 Baseline Data

Baseline and demographic characteristics will be summarized by standard descriptive summaries (e.g. means and standard deviations for continuous variables such as age and percentages for categorical variables such as gender). All covariate data for patients, surgeons, and case will be described and presented in this manner.

Surveys will be summed and scored according to their instructions.

4.2 Analysis of Primary Outcome of Interest

The primary analysis will include all subjects who have completed surveys in their entirety pre-MMS and at 16-weeks after flap placement. A two-tailed paired t-test will be used to compare mean SCI scores between pre-MMS and 16-weeks after flap placement.

4.3 Sample Size and Power

This study will be powered to detect a 5% change from pre-MMS SCI, based upon a SCI validation study that previously reported a pre-MMS score of 60 and standard deviation of 12.8. [7]. A sample size of 145 is needed to achieve 80% power to detect a mean of paired differences of 3.0, with an estimated standard deviation of differences of 12.8, with a significance level (alpha) of 0.05, using a two-tailed paired t-test between pre-MMS SCI and week 16 after flap takedown SCI scores. Anticipating loss of follow up, the final target sample size will be inflated to ~170.

5 Study Administration

5.1 Data Collection and Management

- Consent, patient demographic information, initial SCI study, and surgical details will be completed on paper as part of an intake packet. Intake packets will be faxed to Penn, where trained clinical research fellows will input information into the RedCap, a secure data collection platform. Intake packets will be printed and saved in a secure location at the University of Pennsylvania. Documents for those who completed intake packets but did not go on to receive interpolated flap repair will be destroyed in accordance with HIPAA.

- SCI surveys at 1-week following flap placement, 4-weeks following flap takedown, and 16-weeks following flap takedown will be emailed to patients using RedCap's secure survey administration platform. If a participant fails to complete a survey, they will be contacted via telephone. Trained clinical research fellows may perform the survey over the phone following a detailed script.
- Trained clinical research fellows and the primary investigator will be the only ones with access to RedCap data collection platform.

5.2 Respondent Privacy and Patient Protection

- Patients fulfilling the eligibility criteria for the study will be approached by a Mohs surgeon or clinical staff member (MA or Nurse) while in a private procedure room. The patient will be informed of the study and given the consent documents which they are free to peruse. If they agree to enroll in the study, a copy of the consent document will be given to them to keep.
- Patients will be asked to supply a reliable personal phone number at which they can be reached, and a personal email address. Both of these will be collected in the event that the patient does not wish to return to the office for one or more future follow up appointments. The quality of life surveys will be emailed to the patient, or filled out over the phone.
- We will use study codes on data documents at the data analysis portion of the project and keep a separate document that links the study code to subjects identifying information locked in a separate location and restrict access to this document (e.g., only allowing primary investigators access); Will encrypt identifiable data; Will properly dispose, destroy, or delete study data/ documents; Will limit access to identifiable information; Will securely store data documents within locked locations; Will assign security codes to computerized records. After being downloaded from the secure password-protected RedCap website, all data will be stored on Penn Dermatology's institutionally secured and managed server.

6 References

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