Does the clopidogrel CYP2C19 genotype assay predict postprocedure stenosis in cerebral aneurysms treated with a flow diverter?

Austin J. Allen, BS,1 Aaron Gelinne, MD,2 Nathan S. Quig, MD,2 Samuel Reed, MD,2 Darshan Shastri, MD,2 James P. Ho, MD,3 and Edward Yap, MD1,2

Departments of 1Medical Education, 2Neurosurgery, and 3Neurology, University of North Carolina School of Medicine, Chapel Hill, North Carolina

OBJECTIVE Flow diverters have emerged as a popular modality for treating cerebral aneurysms but require dual antiplatelet therapy (DAPT) after placement. Clopidogrel is a common choice but is a prodrug that some patients may not convert into an active metabolite. The CYP2C19 genotype assay is used to predict activation speed; however, limited data exist showcasing whether this genotype accurately predicts postprocedure complications after flow diversion treatment of cerebral aneurysms. Therefore, the authors sought to characterize whether CYP2C19 genotype correlated with the development of postprocedure intimal hyperplasia (stenosis) after flow diverter placement.

METHODS Medical records were reviewed for patients who underwent flow diverter treatment of cerebral aneurysm at a single academic institution between January 1, 2012, and May 31, 2020. Patient demographics and comorbidities were reviewed alongside CYP2C19 genotype assay, DAPT regimen, and postprocedure angiogram data. Stenosis was defined based on review of angiogram data by two independent physicians.

RESULTS In this review of 120 unique cerebral aneurysms, 102 received DAPT with clopidogrel and 18 received DAPT with an alternative agent. Stenosis was present on 3-month follow-up angiogram for 35/102 (34.3%) aneurysms receiving DAPT with clopidogrel and in 11/18 (61.1%) aneurysms receiving an alternative DAPT regimen (p = 0.031). The CYP2C19 genotype did not correlate with postprocedure stenosis (p = 0.35).

CONCLUSIONS Clopidogrel was a significantly more effective DAPT agent for preventing stenosis when compared to nonclopidogrel DAPT regimens. The clopidogrel CYP2C19 genotype did not predict postprocedure stenosis in this cohort of 120 cerebral aneurysms treated with a flow diverter.

https://thejns.org/doi/abs/10.3171/2023.7.FOCUS23373

KEYWORDS clopidogrel; CYP2C19 genotype; flow diverter; cerebral aneurysms; antithrombotics

Intracranial aneurysms are the most common etiology of nontraumatic subarachnoid hemorrhage. Prevalent in up to 1% of the population, intracranial aneurysms yield significant morbidity and mortality each year.1 Treatment options can be subdivided into two main types: open versus endovascular. Endovascular treatment options include coiling, stent-assisted coiling, and flow diversion. Treatment modality is selected by a combination of aneurysm location and morphology, patient comorbidities, and surgeon preference.1,2

Aneurysms treated with a flow diverter require use of dual antiplatelet therapy (DAPT) to prevent ischemic/thrombotic complications.1 First-line DAPT most commonly consists of once-daily dosing of 81 or 325 mg aspirin alongside an adenosine diphosphate (ADP) receptor inhibitor. Clopidogrel is preferred due to its cost, once-daily dosing (typically 75 mg), and general efficacy.3,4 However, between 21% and 53% of those treated with an aspirin/clopidogrel DAPT regimen have a diminished therapeutic response and are at an increased risk of thrombotic and ischemic complications.5,6

Clopidogrel response is thought to be the result of polymorphisms in the cytochrome P-450 (CYP450) enzymes responsible for activating the prodrug into an active metabolite.7,8 The CYP2C19 genotype assay allows for CYP2C19 alleles to be screened and sorted into drug metabolism phenotypes to help guide DAPT decisions and dosing. Current guidelines suggest considering an alternative ADP receptor inhibitor such as ticagrelor or prasugrel if the CYP2C19 genotype displays a poor or intermediate
metabolism phenotype. Some providers consider doubling the clopidogrel dose for patients with an intermediate or poor metabolism designation, whereas others rely more on alternative methods of assessing DAPT response, such as platelet response units.

Tailoring the DAPT regimen to patients based on CYP2C19 assay findings is currently used in clinical practice, but even with this tailored approach, intimal hyperplasia (stenosis) and other complications are still observed. The role of the CYP2C19 assay has been thoroughly investigated in patients undergoing percutaneous coronary intervention (PCI) with coronary stents; however, this information cannot be directly applied to neurosurgical patient populations because the risk of hemorrhagic complications is significantly higher in cerebral endovascular interventions. A few neurosurgery-specific studies have been published in recent years examining this topic; however, they noted small sample sizes and the need for additional studies to support findings, particularly in relation to the role of the CYP2C19*17 allele. We conducted this retrospective study to assess the correlation between CYP2C19 genotype results and the incidence of chronic stent thrombosis (stenosis) in patients undergoing flow diversion treatment of cerebral aneurysms.

**Methods**

**Subject Identification**

This was a retrospective study of a consecutive series of patients who received a flow diverter for treatment of cerebral aneurysms at a single academic medical center between January 1, 2012, and May 31, 2020. Patients were identified based on a query of our institution’s electronic medical record system. Keywords used to identify patients were “pipeline” and “PED.” These keywords were chosen to identify patients treated with a flow diverter because this is the brand name of the device commonly used at our institution. Patients were eligible for inclusion if they received a flow diverter for treatment of a cerebral aneurysm, had results for the CYP2C19 genetic screening assay, had accessible information about their DAPT regimen prescription, and had an available angiogram for assessment of the flow diverter device. This study was approved by the institutional review board.

**Baseline Characteristics and Clinical Outcomes**

Patient age, sex, and race were recorded. The presence of postprocedure stenosis was determined based on review of an angiogram obtained approximately 6 months after placement of the flow diverter. This was considered to be the primary clinical outcome assessed, given the objective nature of the measurement. Each angiogram was reviewed independently by two board-certified cerebrovascular specialists. For discrepancies in observations about stenosis, both specialists met and reviewed the angiogram to reach a mutual conclusion about the degree of stenosis. For analytical purposes, the quantified percent stenosis was also converted into a qualitative “yes” or “no” for whether any stenosis was present. The anatomical location of each aneurysm was also noted.

Other clinical outcomes were assessed by performing a 30-day review of patient charts for both hemorrhagic and ischemic complications. Hemorrhagic complications were defined as any intracranial hemorrhage noted on imaging alongside a neurological deficit. Ischemic complications were defined as any episode with a neurological deficit noted not to be the result of a hemorrhagic process. Patients with both transient ischemic attacks and more permanent neurological deficits were all included within the ischemic complication group. Due to the low incidence of complications within a relatively small study size, risk-adjusted clinical outcomes were not assessed, and both hemorrhagic and ischemic clinical outcomes were considered to be a secondary study outcome.

**Data Recording and Statistical Analysis**

All study data were obtained from chart review of electronic medical records. Chi-square analysis was used to compare the efficacy of each DAPT agent for preventing the development of stenosis. A threshold of p < 0.05 was used to determine statistical significance. Statistical analyses were performed in RStudio (posit.co).

**Patient Informed Consent**

Consent to pursue this research project was obtained through the University of North Carolina Institutional Review Board. All patients provided consent to undergo treatment. This was a retrospective study so direct consent was not obtained for this particular analysis; however, the standard consent form at our institution includes a waiver to review data for research purposes.

**Results**

**Inclusion Criteria Statistics**

Our search revealed 537 patient charts containing the phrase “pipeline” or “PED.” Manual search of the charts revealed that 123 aneurysms were treated with a flow diverter. Two aneurysms were excluded due to no follow-up diagnostic angiogram after flow diverter placement, and 1 aneurysm was excluded due to pediatric age at the time of flow diverter placement. This left 120 unique aneurysms treated by a flow diverter for inclusion in the study. Of these 120 aneurysms, 111 required only 1 flow diverter to be placed, 7 required 2 flow diverters to be placed on separate procedure dates, and 2 required 3 flow diverters to be placed on separate procedure dates. A summary of how patients were selected for this study can be seen in the flow diagram in Fig. 1.

**Baseline Characteristics and Demographics**

In this cohort of 120 unique aneurysms, 100 (83.3%) were in female patients and 20 (16.7%) were in male patients. The median age was 55 years (IQR 47–63 years). Aneurysms were treated in 71 White patients (59.2%), 29 Black patients (24.2%), 14 Hispanic patients (11.7%), and 6 patients (5.0%) who reported other race or had missing race data (Table 1). The median time to follow-up angiogram after flow diverter placement was 190 days (IQR 177–216 days). Aneurysms were found in anterior circulation in 93 cases (77.5%) and posterior circulation...
in 27 cases (22.5%). Anterior circulation was defined as an aneurysm within the internal carotid artery or direct branches, the middle cerebral artery, or the anterior communicating artery. Posterior circulation was defined as an aneurysm within the vertebral artery, basilar artery, posterior cerebral artery, posterior communicating artery, or posterior inferior cerebellar artery.

Clopidogrel Genotype Options

The CYP2C19 genotype assay reports allelic combinations for the CYP2C19 gene. The most common alleles (1, *2, *3, and *17) are included in the screening assay. The CYP2C19*1 allele is associated with hyperactivation of the prodrug, the CYP2C19*1 allele with normal metabolism, and the CYP2C19*2 and *3 alleles with slower activation. The various different allelic combinations are commonly categorized into 5 different metabolism phenotypes: ultrarapid, rapid, normal, intermediate, and poor (Table 2).

Aneurysms Developing Stenosis

A breakdown of the number of aneurysms that went on to develop postprocedure stenosis based on CYP2C19 genotype is shown in Table 3. Two aneurysms had an ultrarapid clopidogrel metabolizing phenotype. Both of these aneurysms received DAPT containing clopidogrel, and 1 of 2 (50%) of these aneurysms went on to develop stenosis. Twenty-eight patients had a rapid metabolism phenotype; 27 received clopidogrel and 10/27 (37%) went on to develop stenosis. The only patient with a rapid phenotype who received DAPT without clopidogrel developed stenosis. Fifty-nine patients had a normal metabolism phenotype and received DAPT with clopidogrel, and 19 (32.2%) of those developed stenosis. Twenty-nine intermediate metabolizers were identified. Fourteen of 29 received DAPT with clopidogrel, and 5/14 (35.7%) developed stenosis. Eight of 15 (53.3%) of the intermediate metabolizers who received DAPT without clopidogrel developed stenosis. Two patients had a poor metabolism phenotype, and both of these went on to develop stenosis despite receiving DAPT without clopidogrel.

For the 7 patients who had 2 unique cerebral aneurysms treated with a flow diverter, 5 of the 7 patients did
not develop stenosis in either of the aneurysms (n = 10/10 aneurysms without stenosis), and 2 of the 7 patients had 1 of 2 aneurysms develop stenosis (n = 2/4 aneurysms without stenosis).

Of the 74 aneurysms that did not develop stenosis, 67/74 (90.5%) received DAPT with clopidogrel and 7/74 (9.5%) received DAPT without clopidogrel. Even though only 18 of the 120 (15.0%) aneurysms reviewed in this study received DAPT without clopidogrel, 11 of the 46 (23.9%) that developed stenosis received DAPT without clopidogrel. This represents a significantly higher number (23.9%) that developed stenosis received DAPT without clopidogrel, whereas other DAPT regimens developed stenosis, whereas 5/18 (27.8%) accounted for only 5/13 (38.5%) complications. However, other DAPT regimens developed ischemic complications, whereas 5/18 (27.8%) aneurysms receiving other DAPT regimens developed ischemic complications (p = 0.01). Treated aneurysms that went on to develop ischemic complications had a rapid phenotype in 1/13 (7.7%) cases, normal phenotype in 4/13 (30.8%) cases, intermediate phenotype in 7/13 (53.8%) cases, and poor phenotype in 1/13 (7.7%) cases. The rapid and normal phenotype cases all received clopidogrel, the poor phenotype received other DAPT, and the intermediate phenotypes were split—with 3/7 (42.9%) receiving clopidogrel and 4/7 (57.1%) receiving other DAPT.

### Discussion

Clopidogrel is a commonly used antiplatelet agent alongside aspirin to prevent ischemic complications following endovascular procedures. However, because it is a prodrug, not all patients are able to convert it into an active metabolite. The CYP2C19 genotype exists to characterize a patient’s phenotype and likelihood of achieving a therapeutic response to clopidogrel. It has been well established in the cardiac literature that using CYP2C19 genotype screening results in improved treatment outcomes with fewer ischemic complications in patients undergoing PCI. Based on these data, the CYP2C19 genotype is routinely assessed at our institution as a part of the standard clinical protocol for determining a patient’s DAPT regimen. However, prior studies examining the CYP2C19 genotype in patients undergoing neuroendovascular interventions yielded limited overall conclusions about the utility of these treatments in this unique patient group.

Of note, our current clinical protocol is for all patients undergoing flow diverter treatment of cerebral aneurysms to receive CYP2C19 genotype screening. Patients with an ultrarapid, rapid, or normal CYP2C19 genotype are started on a DAPT regimen with clopidogrel. Patients with an intermediate CYP2C19 genotype are started on clopidogrel or an alternative agent based on attending physician preference. Patients with a poor CYP2C19 genotype are started on a DAPT regimen without clopidogrel. Aspirin dosing as part of the DAPT regimen is also decided based on the attending physician’s preference, but is typically chosen based on data suggesting 81 mg daily for patients weighing less than 70 kg or 325 mg daily for patients weighing more than 70 kg.

### TABLE 1. Overview of baseline demographics, timeline of follow-up angiogram, and aneurysm location

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cohort, n = 120</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, no. (%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>100 (83.3%)</td>
</tr>
<tr>
<td>Male</td>
<td>20 (16.7%)</td>
</tr>
<tr>
<td>Age, median (IQR)</td>
<td>55 (47, 63)</td>
</tr>
<tr>
<td>Race, no. (%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>71 (59.2%)</td>
</tr>
<tr>
<td>Black</td>
<td>29 (24.2%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>14 (11.7%)</td>
</tr>
<tr>
<td>Other/missing</td>
<td>6 (5.0%)</td>
</tr>
<tr>
<td>Days to post-FD FU angio, median (IQR)</td>
<td>190 (177, 216)</td>
</tr>
<tr>
<td>Aneurysm location, no. (%)</td>
<td></td>
</tr>
<tr>
<td>Anterior circulation</td>
<td>93 (77.5%)</td>
</tr>
<tr>
<td>Posterior circulation</td>
<td>27 (22.5%)</td>
</tr>
</tbody>
</table>

Angio = angiogram; FD = flow diverter; FU = follow-up.

Anterior circulation was defined as an aneurysm within the internal carotid artery or direct branches, the middle cerebral artery, or the anterior communicating artery. Posterior circulation was defined as an aneurysm within the vertebral artery, basilar artery, posterior cerebral artery, posterior communicating artery, or posterior inferior cerebellar artery.

### TABLE 2. Clopidogrel metabolism phenotype based on CYP2C19 genotype assay results

<table>
<thead>
<tr>
<th>Metabolism Designation</th>
<th>Allelic Composition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrarapid</td>
<td>*17/*17</td>
</tr>
<tr>
<td>Rapid</td>
<td>*1/*17</td>
</tr>
<tr>
<td>Normal</td>
<td>*1/*1</td>
</tr>
<tr>
<td>Intermediate</td>
<td>*1/*2</td>
</tr>
<tr>
<td></td>
<td>*1/*3</td>
</tr>
<tr>
<td></td>
<td>*2/*17</td>
</tr>
<tr>
<td></td>
<td>*3/*17</td>
</tr>
<tr>
<td>Poor</td>
<td>*2/*2</td>
</tr>
<tr>
<td></td>
<td>*2/*3</td>
</tr>
<tr>
<td></td>
<td>*3/*3</td>
</tr>
</tbody>
</table>

* Denotes an abbreviation for each CYP2C19 allele (e.g., ultrarapid is homozygous with 2 copies of allele 17 for the CYP2C19 gene).
Prior Neuroendovascular Studies

In 2016 Lin et al. provided one of the first publications examining correlations between the CYP2C19 genotype and clinical outcomes after a variety of cerebral endovascular interventions (simple coiling, stent-assisted coiling, and Pipeline embolization device) from a prospectively enrolled Australian cohort with 108 patients. They found that individuals with a homozygous CYP2C19*17 allele (ultrarapid phenotype) experienced a significantly increased risk of ischemic complications as compared to other phenotypes. Furthermore, they found that alleles associated with a poor metabolism phenotype (*2 and *3) were not significantly associated with clinical outcomes and clopidogrel response. These results were particularly surprising because the ultrarapid phenotypes were expected to be at increased risk of hemorrhagic complications, whereas the poor metabolizers were expected to be at increased risk of ischemic complications. Although the authors highlighted limitations to this study, these early findings were the first to suggest that the CYP2C19 genotype may be less predictive for patients undergoing neuroendovascular procedures as compared to patients undergoing coronary procedures.

Other studies published after Lin et al.’s have yielded mixed results. Ge et al. published a study of 215 patients from a Chinese cohort in 2017 that showed good correlation between the CYP2C19 genotype and clinical outcomes, including both ischemic and hemorrhagic complications. Saiz-Rodríguez et al. presented results in 2019 from a Spanish cohort with 123 patients, which also showed a similar trend between CYP2C19 genotype and ischemic/hemorrhagic complications. Specifically, ultrarapid metabolizers were more likely to develop hemorrhagic complications, and normal metabolizers were more likely to develop ischemic complications. In early 2023, Zhou et al. published results from a Chinese cohort of 379 patients in which they showed that the CYP2C19 genotype results were unrelated to ischemic events, but that the maximum platelet aggregation induced by ADP measured by light transmission aggregometry did predict which patients developed ischemic complications.

Implications of Results in This Study

Results from this paper showed that there was no significant difference in the percentage of patients who developed stenosis after flow diverter treatment of cerebral aneurysms based on the CYP2C19 genotype alone. Furthermore, our results show that when the CYP2C19 genotype is not considered, DAPT with clopidogrel was significantly more effective at preventing stenosis than other DAPT regimens.

Uncertainty about how to best manage patients with an intermediate CYP2C19 phenotype resulted in the largest direct comparison between patients with the same CYP2C19 phenotype who received different DAPT regimens. Interestingly, patients with an intermediate clopidogrel metabolism phenotype were less likely to develop stenosis when on a DAPT regimen with clopidogrel (5/14 [35.7%] developed stenosis) than those on alternative DAPT regimens (8/15 [53.3%] developed stenosis). Although there was not a significant difference in the percentage of patients developing stenosis (p = 0.34) in the intermediate metabolism phenotype, there was a surprising trend toward clopidogrel being more effective in this subgroup.

Assessment of hemorrhagic and ischemic complications was limited in this study by the small sample size, but showed a modest increase in the rate of intracranial hemorrhage in patients receiving clopidogrel (1.7%) versus other DAPT regimens (0.0%). However, ischemic compli-

### TABLE 3. Number of aneurysms treated with flow diverters that developed postprocedure stenosis, based on a DAPT regimen with or without clopidogrel

<table>
<thead>
<tr>
<th>CYP2C19 Genotype</th>
<th>Aneurysms w/ Genotype</th>
<th>DAPT w/ Clopidogrel</th>
<th>DAPT w/o Clopidogrel</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Aneurysm Count</td>
<td>No. w/ Stenosis</td>
<td>% w/ Stenosis</td>
<td>Aneurysm Count</td>
</tr>
<tr>
<td>Ultrarapid</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>50.0%</td>
</tr>
<tr>
<td>Rapid</td>
<td>28</td>
<td>27</td>
<td>10</td>
<td>37.0%</td>
</tr>
<tr>
<td>Normal</td>
<td>59</td>
<td>59</td>
<td>19</td>
<td>32.2%</td>
</tr>
<tr>
<td>Intermediate</td>
<td>29</td>
<td>14</td>
<td>5</td>
<td>35.7%</td>
</tr>
<tr>
<td>Poor</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Total</td>
<td>120</td>
<td>102</td>
<td>35</td>
<td>34.3%</td>
</tr>
</tbody>
</table>

NA = not applicable. Boldface type indicates statistical significance.

FIG. 2. Percentage of patients receiving DAPT with or without clopidogrel for the group that either did not or did develop stenosis. Of 74 patients who did not develop stenosis, only 9.5% (7/74) received DAPT without clopidogrel, whereas 23.9% (11/46) of patients who did develop stenosis received DAPT without clopidogrel.
cations were observed in only 7.8% of patients treated with clopidogrel versus 27.8% of patients treated with other DAPT regimens.

The prevalence of complications (hemorrhagic, ischemic, and stenosis) from our study cohort was in line with reports from a 2015 meta-analysis published by Briganti et al. for patients undergoing flow diverter treatment of cerebral aneurysms. Hemorrhagic complications occurred in only 1.7% of our cases versus a range of 0%–7.5% of cases in the meta-analysis. Ischemic complications occurred in 10.8% of our cases, which is within the published baseline of 0%–14.2%. We suspect that our rate of reported ischemic complications is on the higher end of the reported range due to inclusion of transient symptoms that later resolved. Although the overall reported rate of stenosis in this paper was 46/120 (38.3%), only 6 of the 120 (5.0%) aneurysms described in our study developed at least 50% stenosis, which is in line with reports of 0%–8.3% developing > 50% stenosis in the meta-analysis. We chose a more liberal definition of stenosis for this study because we believed that an objective measurement from an angiogram provided a better comparison point for assessing DAPT efficacy in our relatively small cohort versus other clinical outcomes (i.e., ischemic and hemorrhagic complications) in which it would be difficult to account for comorbidities and other baseline conditions impacting the likelihood of complication development.

**Limitations and Future Directions**

This study was limited to a retrospective review, with a primary focus on the development of stenosis after placement of flow diverter devices. Stenosis is an important metric for assessing DAPT efficacy, but other clinical outcomes like ischemic and hemorrhagic complications are also important to consider. Although we report results for hemorrhagic and ischemic complications, we acknowledge that the strength of the analysis for these metrics is limited by the small sample size and lack of an analysis controlling for comorbidities. Furthermore, although a statistically significant difference was observed between clopidogrel and other DAPT regimens, the cohort receiving DAPT with an agent other than clopidogrel was composed of only 18 patients.

Our analysis of medication regimen was determined based only on the prescribed regimen and did not account for compliance with taking medications. Notably, alternatives to clopidogrel like ticagrelor are typically more expensive, which could impact patient compliance with different DAPT regimens.

It is also important to note that prior studies have described population-level differences in the frequency of observed CYP2C19 genotypes based on race/ethnicity. There have also been reports of patients from different racial backgrounds with the same CYP2C19 genotype having different clinical responses, which may limit the generalizability of these findings for international readers. However, to our knowledge, no studies on the role of the CYP2C19 genotype in flow diverter outcomes have been published on cohorts treated in the United States.

We did not include other methods of direct platelet function analysis in this study (e.g., maximum platelet aggregation induced by ADP and P2Y12) due to institutional changes in available laboratory assays during the study period. Future studies involving more patients should incorporate multiple modalities of platelet function analysis alongside a robust cost-efficiency analysis of different medication regimens and diagnostic laboratory methods of assessing response to DAPT. The timing of when these laboratory assays are performed and when antiplatelet medications are initiated in patients should also be considered in subsequent analyses.

**Conclusions**

In this retrospective review of cerebral aneurysms treated with a flow diverter at a single academic institution, DAPT regimens with aspirin and clopidogrel were more effective than other antiplatelet agents at preventing stenosis. This was observed even among patients with an
intermediate clopidogrel metabolism phenotype who received DAPT containing clopidogrel. In a limited analysis of clinical outcomes, hemorrhagic complications were slightly more common in patients treated with clopidogrel, whereas ischemic complications were significantly more common in patients receiving other DAPT regimens. Although the power of this study is limited by the small sample size, these results suggest that the CYP2C19 genotype assay may not be as predictive of long-term outcomes for patients undergoing neurovascular procedures as for patients undergoing PCI. Future studies correlating clinical outcomes to the CYP2C19 genotype and other methods of assessing platelet function are warranted to better understand antiplatelet medication optimization for patients undergoing neuroendovascular intervention.

Acknowledgments

University of North Carolina School of Medicine Medical Alumni Affairs: Austin J. Allen participated in and received funding to support work on this study from the 2020 Carolina Medical Student Summer Research Program.

References


article: Allen, Gelinne, Shastri, Ho. Reviewed submitted version of manuscript: Allen, Quig, Shastri, Ho, Yap. Approved the final version of the manuscript on behalf of all authors: Allen. Statistical analysis: Gelinne. Study supervision: Quig, Yap.

Supplemental Information

Previous Presentations

This work was previously presented as an ePoster at the 2021 AANS conference (virtual, August 21–25, 2021).

Correspondence

Austin J. Allen: University of North Carolina School of Medicine, Chapel Hill, NC. austin_allen@med.unc.edu.