Evaluation of Risk Factors for Glaucoma Drainage Device–related Erosions: A Retrospective Case-Control Study

Valerie Trubnik, MD, Camila Zangalli, MD,* Marlene R. Moster, MD,* Thomas Chia, BS,† Mohsin Ali, BS,† Patricia Martinez, MD,* Jesse Richman, MD,* and Jonathan S. Myers, MD**

Purpose: To identify risk factors for glaucoma drainage device (GDD) erosions.

Patients and Methods: In a retrospective comparative case series, medical records of 1013 patients who underwent GDD surgery performed by 5 surgeons between 2006 and 2011 were reviewed. The outcome measures assessed included age, race, sex, contact lens wear, seasonal allergies, medical comorbidities, glaucoma diagnosis, preoperative oral and topical medications, type and number of preoperative surgeries and lasers, concomitant surgeries, tube type and position, patch graft material, and intraoperative use of Avastin, mitomycin-C, or Triescence. The association of variables with erosion status was evaluated using the Fisher exact test for categorical variables and the exact Wilcoxon rank-sum test for continuous variables.

Results: Charts were included from 339 eyes that had complete data sets and at least 6 months of follow-up. Twenty-eight eyes (8.3%) developed conjunctival erosions. The median follow-up time was 2.03 years for the erosion group and 1.71 years for nonerosion group. Erosion was only associated with the presence of concomitant surgical procedures at the time of GDD implantation (35.7% erosion group vs. 17.4% nonerosion group, $P = 0.02$, OR = 2.64). The majority of concomitant surgeries were composed of pars plana vitrectomy (35.0%) and cataract surgery (32.0%). Variables that were suggestive of association with erosion ($P < 0.20$) included smoking (OR = 2.14), pseudoexfoliation glaucoma (OR = 2.71), and history of dry eye syndrome (OR = 2.22).

Conclusion: History of concomitant intraocular surgery with GDD implantation may be a potential risk factor for future erosions.

Key Words: aqueous shunts, glaucoma drainage devices, glaucoma drainage implants, tube shunt, erosion, exposure

(*J Glaucoma* 2013;00:000–000)

Glaucoma drainage devices (GDD) have increased in use and popularity over the past 15 years. They have been shown to be effective in the treatment of refractory glaucoma, in eyes that responded inadequately to other surgical treatments.[1] They are also currently being evaluated as initial incisional surgery in the ongoing Primary Tube versus Trabeculectomy trial.[1–3]

Received for publication January 1, 2013; accepted October 22, 2013.
From the *Wills Eye Institute; and †Department of Medicine, Thomas Jefferson University, Pennsylvania, PA.
Disclosure: The authors declare no conflict of interest.
Reprints: Valerie Trubnik, MD, Wills Eye Institute, Thomas Jefferson University, 840 Walnut Street, Suite 1100, Philadelphia, PA 19106 (e-mail: valerietrubnik@yahoo.com).
Copyright © 2013 by Lippincott Williams & Wilkins
DOI: 10.1097/IJG.0000000000000034

Since the introduction of GDDs 40 years ago, numerous design enhancements and surgical modifications have improved their clinical outcomes and reduced postoperative complication rates.[4] However, GDDs are still foreign devices that are surgically implanted into the eye and therefore associated with the risk of overlying tissue erosion.[5]

Tube erosion has been postulated to be secondary to multiple causes, including immune-mediated inflammation, excessive tension or mechanical rubbing of tissue overlying the tube, poor perfusion, and ischemic damage to the conjunctiva.[6] Multiple studies and case reports have demonstrated the link between tube erosion and endophthalmitis, reenforcing the need to identify potential risk factors for tube erosion. To date there are few studies exploring these risk factors.[7,8]

In this retrospective comparative case-control study, we reviewed preoperative and intraoperative history to identify risk factors that may predispose the eye to GDD erosion.

PATIENTS AND METHODS

After the approval by the Institutional Review Board (IRB) at the Wills Eye Hospital, we performed a retrospective chart review. Cases were identified by a computerized search of the procedural terminology code for implantation of GDDs (66,180) and their repair (66,185). A total of 1013 GDDs were implanted by 5 surgeons between 2006 and 2011. Charts were included from 339 eyes that had complete data sets, which included all the variables listed below and follow-up of at least 6 months. Of the 339 eyes, 28 developed GDD erosions over the same time period.

Patient information was collected from both electronic and paper charts using IRB-approved uniform data collection sheets in full compliance with the Health Insurance Portability and Accountability Act regulation in an anonymous manner. All research methods used were in compliance with the Declaration of Helsinki.

Preoperative data collected included study eye, age, race, sex, length of follow-up, history of smoking, seasonal allergies, contact lens wear, hypertension, asthma, chronic obstructive pulmonary disease, diabetes, rheumatologic conditions, glaucoma diagnosis, type and number of preoperative topical medications, preoperative use of oral or inhaled steroids, preoperative use of immunomodulating oral medications, type and number of preoperative intraocular surgeries, and glaucoma lasers. Intraoperative data collected included type of tube, its position within the eye and quadrant of implantation, use of intraoperative mitomycin-C, Avastin (Genentech Inc., San Francisco, CA), and/or Triescence (Bristol-Myers Squibb Co., New York,

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

NY), concomitant surgical procedures, and patch graft material to cover the tube. Other aspects of surgical method and technique were not evaluated.

The subjects were divided into 2 groups: erosion and nonerosion. Criteria for erosion included both tube and/or plate exposure. This case-control study compared eyes having erosions with eyes that did not, with respect to the distribution of their potential risk factors.

Statistical analysis was performed using SAS 9.2 (SAS Institute Inc., Cary, NC). Categorical variables were summarized with frequencies and percentages. Continuous variables were summarized with means, and minimum and maximum values. The Fisher exact test was used for association of categorical variables with erosion status. The exact Wilcoxon rank-sum test was used to test for associations of continuous variables with erosion. *P*-values for comparisons of groups adjusted for log follow-up time were calculated using logistic regression. No adjustments were made for multiple comparisons.

RESULTS

A total of 339 eyes from 322 patients were included in this study. There were 28 erosions and 311 controls. The race, sex, and mean age was similar in both groups (Table 1). The median follow-up time was 722 days for erosion cases and 610 days for nonerosion controls. Although follow-up time was somewhat longer in the erosion group, the difference in time-to-erosion was not statistically significant ($P = 0.63$).

Primary open-angle glaucoma was the most common type of glaucoma in both the erosion and control groups. Ahmed glaucoma implants (FP7 and S2) constituted the highest number of implanted tubes in both groups (71% in the erosion group and 67% in the control group). Most GDDs were implanted in the superotemporal region (90% in the erosion group and 89.1% in the control group) and into the anterior chamber (89.3% in the erosion group and 90.7% in the control group). The rest of the data on tube location and position are shown in Table 2. The most common patch graft material used was the Tutoplast pericardium patch graft (21/28 in the erosion group and 258/311 in the control).

The only significant association in the study was the presence of concomitant surgical procedures at the time of the GDD implantation (35.7% in the erosion group vs. 17.4% in the nonerosion group, $P = 0.02$, OR = 2.64). The concomitant surgeries included cataract extraction and insertion of an intraocular lens (CE/IOL), orphan trabeculectomy, penetrating keratoplasty, pars plana vitrectomy, bleb needling/revision, keratoprosthesis, cyclophotocoagulation, and IOL exchange or removal. The majority of the concomitant surgeries were composed of pars plana vitrectomy (35.0%) and CE/IOL (32.0%). The type of concomitant surgery that may predispose to erosion was not evaluated for statistical significance due to the small number of eyes in certain subcategories. A summary of risk factors for erosion status is shown in Table 2. The significant association with concomitant procedures should be interpreted with caution, as the *P*-values are not adjusted for multiple comparisons.

Because of the low number of patients with data from multiple eyes, the potential for correlation among eyes from the same subject was ignored in our analysis.

Variables that were suggestive of association with erosion ($P < 0.20$) included smoking (OR = 2.14), pseudoexfoliation glaucoma (OR = 2.71), and history of dry eye syndrome (OR = 2.22). In all of the above cases, the erosion group was more likely to have the risk factor that the nonerosion group.

DISCUSSION

As implantation of GDDs is gaining in popularity and now believed to be surpassing the rate of trabeculectomies,[9] it is vital that we identify the possible risks of the procedure and minimize them. One such risk is the exposure of the GDD. There are few studies in the current literature identifying the risk factors for tube erosion and/or the incidence of erosion. A 2010 meta-analysis of previously published articles by Stewart and colleagues evaluated the timing and incidence of conjunctival tube exposure reported for GDDs. A total of 3255 eyes of 3105 patients were evaluated for an average of 26 months. The overall incidence of tube exposure was 2.0%, with an average rate of exposure of 0.09% per month. The study suggested that the incidence of tube exposure did not differ between the types of implants used and could occur at any time within the first 5 years after implantation. In addition, the authors failed to identify any disparity in the incidence of exposure between the type and the size of the implant. That study, however, was not designed to identify specific risk factors related to patient or implant characteristics that would help predict GDD exposure.[10]

In our study we aimed to identify those elements of the patient's preoperative and intraoperative history that could potentially increase their risk of GDD erosion and subsequent reoperation. We found that having a history of concomitant intraocular surgery with GDD implantation may be a potential risk factor for future erosions. Moreover, other variables such as smoking, dry eye syndrome, and pseudoexfoliation glaucoma may be associated with a higher likelihood of exposure as well.

Exposure of the device can lead to endophthalmitis or an aqueous humor leak resulting in ocular hypotony.[7,11,12] As these adverse outcomes can result in significant patient morbidity, it is imperative that we investigate why these

TABLE 1. Demographics and Length of Follow-up

	Erosion (N = 28)	Nonerosion (N = 311)	Significance (*P*)
Age (y)	69.5 (29-91)	68.5 (33-99)	0.88
Sex (female/male)	11/17 (39.3%/59.7%)	156/155 (50.2%/49.8%)	0.33
Race (C/AA/H/A)	19/7/2 (68%/25%/7%)	170/87/22/7 (60%/30%/8%/2%)	0.91
Median length of follow-up (y)	2.03 (0.751-5.775)	1.71 (0.041-6.003)	0.63

A indicates Asian; AA, African American; C, Caucasian; H, Hispanic.

© 2013 Lippincott Williams & Wilkins

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

TABLE 2. Risk Factors for Erosion

	Erosion (N = 28)	Nonerosion (N = 311)	*P*	*P* Adjusted for Log Follow-up Time
Previous surgeries	1.64 (0-4)	1.70 (0-7)	0.95	0.91
Hx of concomitant surgeries	10 (35.7%)	54 (17.4%)	0.02	0.02
Post-GDD surgeries	0.29 (0-4)	0.23 (0-3)	0.83	0.53
Smoking	5 (17.9%)	28 (9.2%)	0.18	0.19
Seasonal allergies	1 (3.6%)	16 (5.1%)	1.0	0.70
Dry eye syndrome	6 (21.4%)	34 (10.9%)	0.12	0.11
Hypertension	15 (53.6%)	180 (57.9%)	0.69	0.65
Diabetes	6 (21.4%)	83 (26.7%)	0.66	0.55
Rheumatological conditions	2 (7.1%)	17 (5.5%)	0.66	0.74
Oral steroids/immunomodulators	1/1 (3.6%/3.6%)	12/12 (3.9%/3.9%)	1.0/1.0	0.96/0.94
MMC/Avastin/Triescence	3/0/3 (10.7%/0%/10.7%)	35/1/25 (11.3%/0.3%/8.0%)	1.0/1.0/0.72	0.88/0.69/0.66
OAG/CACG/NVG/ UVG/PXG/PG	16/3/2/3/4/0 (57%/11%/7%/11%/14%)	155/45/28/35/18/3 (50%/15%/9%/11%/6%/1%)	0.56/0.78/1.0/ 1.0/0.10/1.0	0.48/0.58/0.74/0.94/0.13/0.48
Contact lens use	1 (3.6%)	10 (3.2%)	1.0	0.92
No. preoperative topical medications				
Steroids	0.25 (0-1)	0.42 (0-2)	0.50	0.29
Restasis	0.07 (0-1)	0.18 (0-1)	1.0	0.52
Glaucoma medications	2.96 (0-4)	3.23 (0-4)	0.67	0.34
NSAIDs	0.11 (0-1)	0.23 (0-1)	0.91	0.47
Tube type				
Baerveldt	6 (21.4%)	92 (21.6%)	0.40	0.50
Ahmed	20 (71.4%)	207 (66.6%)		
Molteno	2 (7.1%)	12 (3.9%)		
Tube location (quadrant)				
ST/IT/SN/IN	25/1/2/0 (90%/3%/7%/0%)	277/18/14/2 (89.1%/5.8%/4.5%/0.64%)	0.81	0.83
Tube position within the eye				
AC/PC/PP	25/1/2 (89.3%/3.6%/7.1%)	282/15/14 (90.7%/4.8%/4.5%)	0.86	0.79
Patch graft material				
Tutoplast	21 (75%)	258 (83%)	0.14	0.31

AC indicates anterior chamber; CACG, chronic angle closure glaucoma; GDD, glaucoma drainage device; IN, inferonasal; IT, inferotemporal; MMC, mitomycin-C; NSAID, non-steroidal anti-inflammatory drug; NVG, neovascular glaucoma; OAG, open angle glaucoma; PC, posterior chamber; PG, pigmentary glaucoma; PP, Pars Plana; PXG, pseudoexfoliative glaucoma; SN, superonasal; ST, superotemporal; UVG, uveitic glaucoma.

erosions occur. There have been several theories postulated in the literature to identify the cause.

Prior or concurrent ocular surgery may induce either conjunctival scarring or thinning leading to erosion. Moreover, surgeries such as a vitrectomy or keratoplasty may influence the rigidity of the eye and predispose the implant to movement within the eye, regardless of whether it is fixated to the globe with sutures or not.[5,13] Byun and colleagues reported that previous ocular surgical procedures elevated the risk for erosion. Those eyes with at least 1 ocular surgery had 9 times the risk of Ahmed GDD erosions than eyes without prior ocular surgery.[14] Unlike Byun's group, our study found that it is the concurrent rather than previous ocular surgery that may be a potential risk factor for GDD exposure.

Prolonged operative time, increased instrumentation, desiccation of conjunctival tissue, and related inflammatory changes associated with combined procedures are all suspected to contribute to the processes underlying the erosion of the GDD. Hence, when evaluating patients for combined procedures such as a phacoemulsification with GDD implantation, it could be theorized that staging the procedures may help minimize the risk of future postoperative erosions.

Studies have also shown that once an implant is exposed, the damaged conjunctiva becomes ischemic and difficult to repair. The recurrence of exposure in these cases is frequent.[5,15] In our study 8/28 (28.5%) eyes reeroded and 75% of those had >2 episodes of erosion. This may suggest that underlying tissue factors, separate from surgical technique may be related to these erosions.

Another theory to explain GDD erosion was suggested by Heuer and colleagues. The authors of that paper postulated that conjunctival tissue and Tenon's capsule degenerate with age, resulting in erosion.[5,6,14,16] However, this study failed to show any significant difference in age between the erosion and nonerosion groups.

Huddleston and colleagues demonstrated that black race, diabetes, previous glaucoma laser procedures, and initial shunt implantation combined with another procedure were associated with a worse outcome after initial shunt exposure repair. They also suggested that having underlying diabetes was associated with a shorter interval between revision and reexposure of the GDD.

Huddleston et al[5] also postulated in their study that certain physical properties of the suture material used for the plate and/or tube fixation or the bulk of the knot itself (or a combination of both) were responsible for the erosions. Compression of small vessels by the suture material may cause local ischemia and apoptosis, leading to implant exposure. Because of the retrospective nature of our study we were not able to identify whether use of specific sutures

© 2013 Lippincott Williams & Wilkins

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

may have been the culprit of exposure. Moreover, kinking of the tube or its vaulting off of the sclera, has also been postulated by some to be a possible reason for tube erosion.[10] This retrospective study could not evaluate either of these possible risk factors.

Owen and colleagues suggested that vascular changes within the conjunctiva of patients with diabetes were similar to those found within their retina and peripheral vasculature. A reduction in the density and caliber of the microvasculature, accompanied by an increase in vessel tortuosity are believed to limit adequate perfusion of the conjunctiva in these patients. These changes can eventually lead to an ischemic conjunctiva that is slower to heal after surgery, less likely to resist the proposed factors causing exposure, and more likely to reexpose after repair.[17] However, our study failed to show that diabetes, hypertension, or rheumatologic conditions such as lupus or rheumatoid arthritis, had any effect on increasing the incidence of implant exposure.

Other research has shown that chronic use of topical ocular medications may result in poor conjunctival status. Unhealthy conjunctiva may be less able to maintain its integrity when subjected to the stress of the underlying implant and any inflammatory response that may result. Preservatives in glaucoma drops are believed to damage the conjunctiva through processes such as desiccation, instability of tear film, and loss of goblet cells. It is suspected that an increase in the number of drops may worsen this process.[18] Our study did not find the use of multiple preoperative drops to be a risk factor for exposure.

We also did not find a significant difference between the patch grafts used for covering the GDDs during the initial procedure.[19] Similarly, Smith et al[15] demonstrated that no material was more prone to erosion than another when comparing donor sclera, pericardium, and dura mater with a mean follow-up of 33 months. Raviv and colleagues retrospectively reviewed 44 eyes with GDD implantations accompanied by pericardial patch grafting and found no cases of tube erosion with an average follow-up of 10.2 months.[20,21] It is plausible that we may not have found a difference in the rates of erosion between grafts due to the absence of certain types of grafts in the erosion category (ie, 0 cases of sclera patch grafts, amniograft, and/or sclera tunnel in the erosion group). Hence, we were unable to compare the actual materials to each other and assess them for risks of erosion separately.

There have been several studies published on the position of the implant being a risk factor for exposure. Pakravan and colleagues noted that inferior quadrant implantation leads to more complications, including erosion over the plate. The authors postulated that this may be secondary to a shallower space within the inferior fornix and less conjunctiva available to cover the implant, thereby possibly increasing the rate of wound dehiscence.[6] Our results did not suggest an association between inferior placement of the tube and exposure. However, the study had only a small number of GDDs implanted in the inferior quadrant in both the erosion and control group and that may have been the reason we did not find an association (1/28 in the erosion group and 20/311 in the control group).

We restricted this investigation to evaluation of potential risk factors of GDD erosion and did not assess surgical outcomes. Furthermore, surgical technique was not evaluated as a potential risk factor. As our data was collected from 5 surgeons, we believe that this poses one of the primary limitations of the study. We were also only able to evaluate charts that had complete data sets of the variables of interest. Hence, only those patients were selected to be part of the study. Moreover, there were certain patients that were not included due to loss to follow-up at Wills Eye Hospital, though records indicate that they continued to see their comprehensive ophthalmologists. The follow-up data from the other ophthalmologists were not readily available or accessible. These patients can only be presumed to be doing well, as they did not return for further specialty glaucoma care. This may have biased our results, as patients with erosions may have been more likely to have data available for analysis because they were sent back. Conversely, it is possible that some patients suffering erosions chose to seek care elsewhere.

GDD exposure is an infrequent occurrence making it more difficult to amass large numbers for analysis. The limited numbers available may increase the chance that the trends observed (eg, dry eye syndrome or pseudoexfoliation glaucoma) are by chance rather than true causal effect.

In conclusion, this is the first single-site study to our knowledge that extensively evaluates the risk factors for GDD erosions. Our findings demonstrate that concomitant surgeries are a potential risk factor for these events. Further investigation and more extensive data collection may be necessary to elucidate these associations. This study marks the first step in an investigative effort to identify those aspects of a patient's history that may alert the surgeon to potentially avoidable postoperative complications of this common glaucoma procedure.

REFERENCES

1. Gedde SJ, Parrish RK, Budenz DL, et al. Update on aqueous shunts. *Exp Eye Res*. 2011;93:284–290.
2. Gedde SJ, Schiffman JC, Feuer WJ, et al. Treatment outcomes in the tube versus trabeculectomy (TVT) study after five years of follow-up. *Am J Ophthalmol*. 2012;153:789–803, e2.
3. Panarelli JF, Gedde SJ, Schiffman JC, et al. Clinical outcomes of primary tube shunt surgery versus primary trabeculectomy with mitomycin-c (MMC). European Glaucoma Society Annual Meeting, Tivoli Congress Center, Copenhagen, Denmark, June 20, 2012. Poster P5.80.
4. Patel S, Pasquale LR. Glaucoma drainage devices: a review of the past, present, and future. *Semin Ophthalmol*. 2010;25:265–270.
5. Huddleston SM, Feldman RM, Budenz DL, et al. Aqueous shunt exposure: a retrospective review of repair outcome. *J Glaucoma*. 2011;22:433–438.
6. Pakravan M, Yazdani S, Shahabi C, et al. Superior versus inferior Ahmed glaucoma valve implantation. *Ophthalmology*. 2009;116:208–213.
7. Gedde SJ, Scott IU, Tabandeh H, et al. Late endophthalmitis associated with glaucoma drainage implants. *Ophthalmology*. 2001;108:1323–1327.
8. Lama PJ, Fechtner RD. Tube erosion following insertion of a glaucoma drainage device with a pericardial patch graft. *Arch Ophthalmol*. 1999;117:1243–1244.
9. Ramulu PY, Corcoran KJ, Corcoran SL, et al. Utilization of various glaucoma surgeries and procedures in Medicare beneficiaries from 1995 to 2004. *Ophthalmology*. 2007;114:2265–2270.
10. Stewart WC, Kristoffersen CJ, Demos CM, et al. Incidence of conjunctival exposure following drainage device implantation in patients with glaucoma. *Eur J Ophthalmol*. 2010;20:124–130.
11. Nguyen QH. Avoiding and managing complications of glaucoma drainage implants. *Curr Opin Ophthalmol*. 2004;15:147–150.
12. Sarkisian SR. Tube shunt complications and their prevention. *Curr Opin Ophthalmol*. 2009;20:126–130.

© 2013 Lippincott Williams & Wilkins

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

13. Fechter HP. What's new on the tube?: recent trends, updates, and controversy in aqueous shunt surgery. *Glaucoma Today*. 2012; (January/February 2012): 14–16.
14. Byun YS, Lee NY, Park CK. Risk factors of implant exposure outside the conjunctiva after Ahmed glaucoma valve implantation. *Jpn J Ophthalmol*. 2009;53:114–119.
15. Smith MF, Doyle JW, Ticrney JW. A comparison of glaucoma drainage implant tube coverage. *J Glaucoma*. 2002;11:143–147.
16. Heuer DK, Budenz D, Coleman A. Aqueous shunt tube erosion. *J Glaucoma*. 2001;10:493–496.
17. Owen CG, Newsom RSB, Rudnicka AR, et al. Vascular response of the bulbar conjunctiva to diabetes and elevated blood pressure. *Ophthalmology*. 2005;112:1801–1808.
18. Pisella PJ, Pouliquen P, Baudouin C. Prevalence of ocular symptoms and signs with preserved and preservative free glaucoma medication. *Br J Ophthalmol*. 2002;86:418–423.
19. Lankaranian D, Reis R, Henderer JD, et al. Comparison of single thickness and double thickness processed pericardium patch graft in glaucoma drainage device surgery: a single surgeon comparison of outcome. *J Glaucoma*. 2008;17:48–51.
20. Ainsworth G, Rotchford A, Dua HS, et al. A novel use of amniotic membrane in the management of tube exposure following glaucoma tube shunt surgery. *Br J Ophthalmol*. 2006;90:417–419.
21. Raviv T, Greenfield DS, Liebmann JM, et al. Pericardial patch grafts in glaucoma implant surgery. *J Glaucoma*. 1998;7:27–32.

© 2013 Lippincott Williams & Wilkins

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.