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PGY1 CRC IRB proposal

Study Purpose and Rationale

Pericardial effusion is a potentially dangerous accumulation of fluid in the pericardial space that can lead to cardiac tamponade, shock, and sometimes death. In general, there are surgical based approaches [1-7] and percutaneous based approaches [8-13] to pericardial fluid drainage. However, the optimal treatment for symptomatic pericardial effusions, whether percutaneous catheter drainage (PCD) or open surgical drainage (OSD), remains controversial despite several retrospective analyses that have attempted to clarify this issue [14-17]. One recent three year retrospective chart review of all patients who had drainage of symptomatic pericardial effusion via PCD or OSD at Columbia University Medical Center revealed no significant difference in either 30-day mortality or 1-year Kaplan-Meier survival between patients who had the two procedures. However, the study did reveal that PCD was associated with a higher rate of recurrence but a lower rate of procedure-related complications [18]. Further research with a larger number of patients will help clarify more definitively the relative safety and efficacy of these two approaches.

Study Design and Statistical Analysis:

It is our hypothesis that patients undergoing PCD and OSD for symptomatic pericardial effusion will have comparable short term (30 day) and long term (1 year) survival after the procedures. We also believe that PCD will result in fewer peri-procedural complications, but will more frequently require repeat drainage.

To evaluate this issue, we will conduct a retrospective, multi-institution study examining patients who have been treated with either PCD or OSD for symptomatic pericardial effusion. Since this study is retrospective, there will be no randomization, as the patients have already been treated. The primary endpoint will be 30 day survival, and secondary endpoints will include 1 year survival, peri-procedural complications, and effusion recurrence requiring repeat drainage within 90 days.

The patients will be identified by using CPT billing codes for the procedures of interest (i.e. PCD and OSD). Once the patients have been identified, all patient charts will be evaluated independently but one interventional cardiologist and one cardiothoracic surgeon. The two reviewers will be blinded to the ultimate treatment pursued (PCD or OSD). The two reviewers will determine whether there is clear indication for PCD or OSD or whether the patient could have gone for either procedure. If both agree that a specific indication exists for one procedure over the other, that patient will not be considered. If they agree that the patient could have gone to either treatment arm, that patient will be included in analysis. If they disagree, a third reviewer will determine whether the patient should be included or not.

For all patients, we will collect baseline characteristics, procedural characteristics, procedure-related complications, effusion recurrence requiring repeat drainage within 90 days, 30-day post-procedural survival, and date of death. Baseline characteristic will be compared using Fisher's exact test of chi-squared for proportions and the student t-test for continuous variables. Logistic regression will be used to estimate the association of initial treatment strategy with 30-day procedural outcomes controlling for baseline characteristics that were statistically different between groups. Actuarial survival will be calculated using the method of Kaplan and Meier and compared by initial treatment strategy using the log rank test. Cox proportional

hazards modeling will be used to adjust for baseline characteristics that were statistically different between treatment groups.

To estimate the number of patients needed to evaluate this question, we will use data from the aforementioned recent retrospective chart review comparing PCD and OSD at CUMC. In this study, the 30-day mortality after these procedures was 18.1% and 19.8%, respectively. Using this data as guidance, we will want to demonstrate that the difference in 30-day mortality is less than a pre-defined, clinically-significant difference of 5% (i.e. from 15% to 20%). Using the method of chi-square, we will need to enroll about 962 patients in each treatment arm. However, we will need to review a larger number of charts, as we will want to exclude those patients for whom a clear indication for one procedure exists, for instance those patients with a loculated pericardial effusion which cannot be accessed via PCD. Estimating that about 10% of patients will fall into this category, we will need to enroll about 1,070 patients in each arm.

Study Procedures:
This study will involve only retrospective analysis of data, and all procedures being evaluated have already occurred whether or not the individual was participating in this research project. A list of patients who have undergone the procedures listed above as indicated by CPT codes will be compiled by the Departments of Cardiology and Thoracic Surgery. Patient names and MRNs will be entered into a secure and password protected database. Patient MRNs will be entered into the electronic medical record (i.e. Webcis and Eclipsys) to gather the appropriate data listed above. When necessary, paper charts will also be reviewed to gather data listed above.

Study Drugs or Devices: N/a

Study Questionnaires: N/a

Study Subjects:
We will be identifying all adult patients over 18 years of age who underwent either PCD or OSD for symptomatic pericardial effusion at CUMC and other institutions. This study will include both men and women regardless of race, ethnicity, socioeconomic background, or religion. Patients will be excluded if the screening process outlined above determines that they were not eligible for either procedure, and instead had indication for one procedure over another.

Recruitment: N/a

Confidentiality
All data will be stored on a secure password protected computer in a password protected file. No data will be transmitted to any other site, and all data will be maintained in an electronic form.

Potential Conflict of Interest: N/a

Potential Risks
This study poses minimal risk to the possibility of an unintended breech of patient confidentiality. In order to minimize this risk, the information stored in the project database will be handled with confidentiality and security protocols as outlined above. Furthermore, all

identifying patient information that could be used to identify subjects as a participant in the project will not be used in any published material.

Potential Benefits
There are no direct benefits to participating in the study, as all procedures have occurred in the past. An indirect potential benefit of the study is that it may provide insight into improving current protocols and thereby positively benefit future patients.

Alternatives
This is a retrospective study, and patients have already received their interventions/treatments independent of and prior to this study.

References

1. Larrey EL. New surgical procedure to open the pericardium in the case of fluid in the cavity. Clin Chir 1829; 36: 303–37.

2. Vaitkus PT, Herrmann HC, LeWinter MM. Treatment of malignant pericardial effusion. JAMA 1994; 272: 59–64.

3. Press O, Livingston R. Management of pericardial effusion and tamponade. JAMA 1987;257:1088–92.

4. Miller JI, Mansour KA, Hatcher CR. Pericardiectomy: current indications, concepts and results in a university center. Ann Thorac Surg 1982;34:40–5.

5. Piehler JM, Pluth JR, Schaff HV, et al. Surgical management of effusive pericardial disease: influence of extent of pericardial resection on clinical course. J Thorac Cardiovasc Surg 1985;90:506–16.

6. Hazelrigg SR, Mack MJ, Landreneau RJ, et al. Thoracoscopic pericardiectomy for effusive pericardial disease. Ann Thorac Surg 1993;56:792–5.

7. Shapira OM, Aldea GS, Fonger JD, Shemin RJ. Videoassisted thoracic surgical techniques in the diagnosis and management of pericardial effusion in patients with advanced lung cancer. Chest 1993;104:1262–3.

8. Kopecky SL, Callahan JA, Tajik J, Seward JB. Percutaneous pericardial catheter drainage: report of 42 consecutive cases. Ann J Cardiol 1986;58:633–5.

9. Celermajer DS, Boyer MJ, Bailey BP, Tattersall MHN. Pericardiocentesis for symptomatic malignant pericardial effusion: a study of 36 patients. Med J Aust 1991;154:19–22.

10. Ziskind AA, Pearce C, Lemmon CC, et al. Percutaneous balloon pericardiotomy for the treatment of cardiac tamponade and large pericardial effusions: description of technique and report of the first 50 cases. J Am Coll Cardiol 1993;21:1–5.

11. Lemmon CC, Ziskind AA. Percutaneous balloon pericardiotomy: nonsurgical alternative for treating malignancy-related pericardial effusions. Card B Rev 1993;10:53–9.

12. Di Segni E, Lavee J, Kaplinsky E, Vered Z. Percutaneous balloon pericardiostomy for the treatment of cardiac tamponade. Eur Heart J 1995;16:184–7.

13. Shepherd FA, Morgan C, Evans WK, Ginsberg JF, Watt D, Murphy K. Medical management of malignant pericardial effusion by tetracycline sclerosis. Am J Cardiol 1987;60: 1161–6.

14. Susini G, Pepi M, Sisillo E, Bortone F, Salvi L, Barbier P, Fiorentini C. J. Percutaneous pericardiocentesis versus subxiphoid pericardiotomy in cardiac tamponade due to postoperative pericardial effusion. Cardiothorac Vasc Anesth. 1993 ;7(2):178-83.

15. Allen KB, Faber LP, Warren WH, Shaar CJ. Pericardial effusion: subxiphoid pericardiostomy versus PCD. Ann Thorac Surg. 1999; 67(2): 437-40.

16. McDonald et al. Comparison of Open Subxiphoid Pericardial Drainage With PCD for Symptomatic Pericardial Effusion. Ann Thorac Surg 2003;76:811– 6

17. Ashikhmina et al. Pericardial Effusion After Cardiac Surgery: Risk Factors, Patient Profiles, and Contemporary Management. Ann Thorac Surg 2010;89:112– 8

18. Percutaneous Pericardiocentesis vs Pericardial Window in the Treatment of Symptomatic Pericardial Effusions: Recurrence and Complication Rates. A.Garvey Rene, Yehuda Edo Paz, Adam Saltzman, Philip Green, Ahmed Hassanein, Leroy Rabbani. 2011 TCT Annual Meeting abstract.