I. PROJECT DESCRIPTION

Be as explicit as possible in your description. Please refer to the above instructions which outline the criteria by which applications are reviewed. Be sure to include the following in your outline of the project, not to exceed the available space (approximately 2 – 2 ½ pages).

Background and Hypothesis:
Today, there is an overwhelming consensus on surgical resection being the backbone of curative therapy of gastric adenocarcinoma [1-3]. There has been recent interest in developing adjuvant strategies to improve outcomes, particularly with the addition of chemotherapy and radiation therapy. Adjuvant radiation therapy alone remains unproven as gastric cancer is generally considered to be a relatively radioresistant cancer [4]. The British Stomach Cancer Group conducted a randomized trial to assess adjuvant external beam radiation therapy (EBRT). The study randomly assigned 436 patients who had undergone gastric resection for stage II and III disease to no further therapy, adjuvant EBRT, or adjuvant chemotherapy. Five-year locoregional recurrence was significantly lower in the adjuvant EBRT arm (10% versus 27%) [5]. Attention has also turned to adjuvant chemotherapy and multiple meta-analyses have demonstrated a modest benefit, if any, for adjuvant chemotherapy [6-10]. Also, the British MAGIC (Medical Research Council Adjuvant Gastric Infusional Chemotherapy) study by Cunningham, et al., demonstrated a significant overall survival benefit that favored perioperative ECF chemotherapy regimen (epirubicine, cisplatin, and continuous 5-FU infusion) versus surgery alone [11]. It is known that relapses occur locally, regionally and distantly in most patients that underwent a curative resection of gastric cancer based on data revealed from re-operation and autopsy studies [12-14]. Attention has also focused on combined adjuvant chemotherapy and radiation therapy in order to achieve better control of local and distant micrometastases. Studies that compare mortality for patients with clinically resectable gastric adenocarcinoma have suggested favorable mortality rates for certain treatments over others. The Intergroup 0116 study by MacDonald, et al. showed a significant benefit in overall survival with adjuvant chemoradiotherapy (CRT) consisting of 45 Gy of radiotherapy combined with fluorouracil (5-FU) and leucovorin, versus surgery alone [15].

While both the Cunningham and MacDonald studies described improved mortality rates for the use of adjuvant therapy versus surgery alone, no comparisons of mortality rates have been made between patients receiving surgery and chemotherapy versus patients receiving surgery and chemoradiotherapy. This study’s goals are to compare mean survival rates and relative risks for death in patients with gastric adenocarcinoma treated with surgical resection followed by chemotherapy (S+CHR) or treated with surgery without (S+CH) radiation therapy. For comparison, patients treated with surgical resection alone (SO) will also be included.

Goal 1: Although improved mortality rates have been described for patients receiving adjuvant therapy (S+CHR or S+CH) versus surgery alone (SO), the first goal of this study will be looking to establish that pattern in our data population.
Goal 2: Evaluate failure patterns for patients receiving adjuvant therapy (S+CHR or S+CH) versus surgery alone (SO).

Goal 3: Determine optimal therapy for definitive management of patients with gastric cancer.

Experimental Design and Methods:
IRB approval has been obtained as of March 27, 2016. The research study will consist of a retrospective chart review of pathologically confirmed, resected invasive gastric adenocarcinoma from January, 1999 to December, 2013 will be performed from pathology databases, treatment and billing records, and tumor registries from the University of Washington Medical Center (UWMC), Harborview Medical Center (HMC), and the Seattle Cancer Care Alliance (SCCA). The review will exclude patients with in situ gastric adenocarcinoma, previous malignancies, or concurrent malignancies. Patients receiving treatment as a palliative rather than a curative measure will also be excluded.

Data Collection: The following information will be collected from patients’ medical records: demographic data, cancer diagnosis and date of diagnosis, cancer stage at diagnosis, tumor stage, nodal involvement, treatment modality, and mortality status. Patient charts and the Social Security Death Index will be used to determine the date of death for a deceased patient. Staging data will be obtained through the tumor registries at UWMC, HMC and SCCA.

Data Analysis: The included patient population will be further divided into the three experimental categories (SO, S+CH, S+CHR) using the information from the chart. Failure patterns will be evaluated using data from patient chart. The data will be analyzed to calculate 2-year, 3-year, and 5-year survival rates, create Kaplan-Meier Survival curves to estimate mean survival times for patients in each treatment group, and conduct Cox Regression analyses, controlling for sex, race, cancer stage, and age at diagnosis by quartile, in order to determine any statistically significant differences in mortality between treatments. SPSS Version 17.0 (SPSS Inc., Chicago, Illinois) to conduct the analysis and consider p<0.05 as significant.

Relevance:
Gastric cancer is the fourth most common cancer worldwide and is the second leading cause of cancer-related death [16]. The NCI estimated 24,590 new gastric cancer diagnoses in 2015 with 10,720 deaths [16]. Although mortality from gastric cancer is relatively rare in the United States, it is far more common in other parts of the world [16]. While the overall incidence of gastric cancer is decreasing, the incidence of adenocarcinoma of the gastric cardia and the lower esophagus is increasing in most of the developed Western populations [17-19]. We hope this study establishes and supports the most appropriate treatment modality for an aggressive and widespread disease. These results could provide oncologists an improved method to treat gastric adenocarcinoma and improve mortality rates.

References


