Carotid Endarterectomy in Asymptomatic Patients With Limited Life Expectancy

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Background and Purpose—Data from randomized trials assert that asymptomatic patients undergoing carotid endarterectomy (CEA) must live 3 to 5 years to realize the benefit of surgery. We examined how commonly CEA is performed among asymptomatic patients with limited life expectancy.

Methods—Within the American College of Surgeons National Quality Improvement Project we identified 8 conditions associated with limited life expectancy based on survival estimates using external sources. We then compared rates of 30-day stroke, death, and myocardial infarction after CEA between asymptomatic patients with and without life-limiting conditions.

Results—Of 12,631 CEAs performed in asymptomatic patients, 2,525 (20.0%) were in patients with life-limiting conditions or diagnoses. The most common conditions were severe chronic obstructive pulmonary disease and American Society of Anesthesiologists Class IV designation. Patients with life-limiting conditions had significantly higher rates of perioperative complications, including stroke (1.8% versus 0.9%, P<0.001), death (1.4% versus 0.3%, P<0.001), and stroke/death (2.9% versus 1.1%, P<0.001). Even after adjustment for other comorbidities, patients with life-limiting conditions were nearly 3 times more likely to experience perioperative stroke or death than those without these conditions (OR, 2.8; 95% CI, 2.1–3.8; P<0.001).

Conclusion—CEA is performed commonly in asymptomatic patients with life-limiting conditions. Given the high rates of postoperative stroke/death in these patients as well as their limited life expectancy, the net benefit of CEA in this population remains uncertain. Health policy research examining the role of CEA in asymptomatic patients with life-limiting conditions is necessary and may serve as a potential source for significant healthcare savings in the future. (Stroke. 2012;43:00-00.)

Key Words: appropriate ■ asymptomatic ■ carotid endarterectomy ■ life expectancy

Evidence supporting carotid endarterectomy (CEA) for the treatment of asymptomatic cerebrovascular disease is well established, because several randomized trials have demonstrated a significant reduction in stroke with CEA as compared with medical treatment alone.1 In terms of establishing “appropriate” candidates for CEA, the Society for Vascular Surgery guidelines state that asymptomatic patients with ≥60% carotid artery stenosis should be considered for CEA only when life expectancy is >3 years and perioperative stroke/death risk is <3%.2 Similarly, other professional societies, including the American Heart Association, the American Stroke Association (ASA), and the American Academy of Neurology, stress the importance of assessing life expectancy before pursuing CEA in neurologically asymptomatic patients, asserting that appropriate candidates have a life expectancy >5 years.3–6 Furthermore, the American Academy of Neurology only supports CEA for asymptomatic disease if patients are <75 years of age.6

Although slight differences may exist regarding the exact definition of “appropriate” patient selection criteria for CEA, most physicians would agree that asymptomatic patients with life-limiting conditions who are unlikely to survive long enough to realize the benefit of CEA are “inappropriate” candidates for carotid revascularization. However, it remains unclear how commonly patients with life-limiting conditions might be offered surgery in real-world practice.

The purpose of our study was to examine use and outcomes of CEA in a large cohort of asymptomatic patients with and without life-limiting conditions using a national data set representing actual practice.
Methods

Data and Databases
We studied all patients undergoing CEA in the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) Registry between 2007 and 2009. The American College of Surgeons NSQIP prospectively collects data on >200 variables pertaining to patient characteristics, comorbid conditions, operative details, and 30-day postoperative outcomes for a variety of surgical procedures. In 2007, data were collected from 211 407 cases at 186 sites. By 2009, these numbers had increased to 336 190 cases at 237 sites. More information about American College of Surgeons NSQIP is available at www.acsnsqip.org.

Establishing a Cohort
To establish a cohort of patients undergoing CEA for asymptomatic stenosis, we used Current Procedural Terminology code 35301 to identify patients in the registry who underwent CEA between 2007 and 2009. All CEAs performed concomitant with other procedures (defined as an additional operation performed by a different surgical team such as combined coronary artery bypass grafting/CEA) were excluded. Symptomatic status was then assigned to any subject with a history of cerebrovascular accident with or without neurological deficit or a history of transient ischemic attack (TIA). All remaining cases were defined as asymptomatic.

Next, to identify patients undergoing CEA who also had life-limiting conditions, we evaluated all descriptive patient level covariates in NSQIP and selected those associated with a predicted 5-year mortality ≥40%. Because long-term survival data are not available in NSQIP, we used external sources (such as published medical literature and national registries) to estimate the 3- and 5-year mortality rates of patients with each individual life-limiting condition. The life-limiting conditions used to define our cohort included disseminated cancer, advanced liver disease, symptomatic congestive heart failure, dialysis dependence, and severe chronic obstructive pulmonary disease (COPD). In addition to these medical diagnoses, we also included age ≥90 years, do-not-resuscitate status, and patients designated as ASA Class IV, a preoperative designation assigned by the operating anesthesiologist that implies a patient has “severe systemic disease that is a constant threat to life.” Although the designation of ASA Class IV is not a diagnosis, we characterized this variable as descriptive of the patient’s overall risk for surgery in the perioperative period.8–10 Table 1 lists the predicted 3- and 5-year mortality rates for patients with each condition (operational definitions for each condition are displayed in online-only Data Supplement I; http://stroke.ahajournals.org). We found that predicted 3-year mortality rates ranged from 37% for patients with severe COPD to 76% for patients with disseminated cancer. Predicted 5-year mortality rates were >46% for all life-limiting conditions. Of note, long-term mortality data pertaining to do-not-resuscitate status were not available.

Comparison Between Patients With and Without Life-Limiting Conditions
We compared patient characteristics such as age and comorbidities between patients with and without life-limiting conditions using t tests (for continuous variables) and χ² with Fisher exact correction (for categorical variables) to identify statistically significant differences.

Next, to study surgeon and hospital characteristics associated with selecting patients with life-limiting conditions for CEA in this observational data set, we examined rates of CEA by surgeon teaching status (teaching/nonteaching).

Finally, we compared rates of stroke, death, the combined outcome stroke/death, and postoperative myocardial infarction (defined as a new transmural acute myocardial infarction occurring during surgery or within 30 days, manifested by new Q-waves on electrocardiogram) between patients with and without life-limiting conditions. We found that predicted 3-year mortality rates were 76% for patients with disseminated cancer. Predicted 5-year mortal-

Table 1. Predicted 3- and 5-Y Mortality for Patients With Life-Limiting Conditions and the Associated Reference Used to Estimate Mortality

<table>
<thead>
<tr>
<th>Life-Limiting Condition</th>
<th>Predicted 3-Y Mortality, %</th>
<th>Predicted 5-Y Mortality, %</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disseminated cancer</td>
<td>76</td>
<td>83</td>
<td>Surveillance, Epidemiology, and End Results (SEER) Program¹¹</td>
</tr>
<tr>
<td>Advanced liver disease</td>
<td>63</td>
<td>80</td>
<td>Survival data based on Child-Turcotte criteria¹²</td>
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<tr>
<td>Symptomatic CHF</td>
<td>62</td>
<td>69</td>
<td>Framingham Heart Study¹³</td>
</tr>
<tr>
<td>Dialysis dependence</td>
<td>50</td>
<td>67</td>
<td>United States Renal Data System (USRDS) Annual Data Report¹⁴</td>
</tr>
<tr>
<td>Age ≥90 y</td>
<td>41</td>
<td>62</td>
<td>National Vital Statistics Report, 2006 data¹⁵</td>
</tr>
<tr>
<td>ASA Class IV</td>
<td>41</td>
<td>57</td>
<td>Vinkkunen et al, 2009¹⁶</td>
</tr>
<tr>
<td>Severe COPD</td>
<td>37</td>
<td>46</td>
<td>Third National Health and Nutrition Examination Survey¹⁷</td>
</tr>
<tr>
<td>Do not resuscitate (DNR)*</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

CHF indicates congestive heart failure; ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease.

*Data pertaining to DNR status were not available.

We used multivariable logistic regression to examine the association between 30-day stroke/death rates and other patient-level comorbidities such as diabetes, smoking, or hypertension. These results were reported as ORs with surrounding 95% CIs in online-only Data Supplement II.

Table 2. Characteristics Between Patients With and Without Life-Limiting Conditions Undergoing Carotid Endarterectomy for Asymptomatic Carotid Stenosis

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>Yes Life-Limiting Condition (N=2525)</th>
<th>No Life-Limiting Condition (N= 10 106)</th>
<th>P Value</th>
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<tr>
<td>Age, %</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>&lt;65 y</td>
<td>20.2</td>
<td>23.7</td>
<td></td>
</tr>
<tr>
<td>65–70 y</td>
<td>17.7</td>
<td>18.4</td>
<td></td>
</tr>
<tr>
<td>70–75 y</td>
<td>20.1</td>
<td>19.4</td>
<td></td>
</tr>
<tr>
<td>75–80 y</td>
<td>19.4</td>
<td>19.1</td>
<td></td>
</tr>
<tr>
<td>&gt;80 y</td>
<td>22.7</td>
<td>19.5</td>
<td></td>
</tr>
<tr>
<td>Male, %</td>
<td>57.4</td>
<td>57.5</td>
<td>0.896</td>
</tr>
<tr>
<td>Race, %</td>
<td>0.299</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>46.9</td>
<td>38.8</td>
<td></td>
</tr>
<tr>
<td>Black, Hispanic, other</td>
<td>53.1</td>
<td>61.2</td>
<td></td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>30.9</td>
<td>26.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coronary artery disease, %</td>
<td>47.8</td>
<td>35.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>87.5</td>
<td>85.2</td>
<td>0.002</td>
</tr>
<tr>
<td>Smoker, %</td>
<td>34.2</td>
<td>24.3</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Results

Patient Characteristics by the Presence or Absence of a Life-Limiting Condition

Overall, 22,696 isolated CEAs were recorded in NSQIP between 2007 and 2009. More than half of CEAs (55.7% [12,631]) were performed in patients with asymptomatic carotid stenosis, whereas the remaining 44.3% (10,065) procedures were performed in patients with a documented history of cerebrovascular accident or TIA.

Among CEAs in asymptomatic patients (n=12,631), 20.0% (2,525) were performed in patients who also had at least 1 life-limiting condition. Patients with life-limiting conditions were, on average, slightly older (mean age, 72 years versus 71 years; P<0.001) with more baseline comorbidities (independent of those categorized as life-limiting comorbidities). For example, patients with life-limiting conditions had a higher incidence of diabetes (30.9% versus 26.6%, P<0.001), coronary artery disease (47.8% versus 35.2%, P<0.001), and hypertension (87.5% versus 85.2%, P=0.002; Table 2). The most common conditions occurring in asymptomatic patients were ASA Class IV (10.2% of all asymptomatic CEAs), severe COPD (0.9%), and dialysis dependence (0.9%; Figure 1). Finally, nearly 3% (n=369) of CEAs were performed in patients who had >1 life-limiting condition.

Outcomes by the Presence or Absence of a Life-Limiting Condition

Overall, 1.4% (182) of all asymptomatic patients undergoing CEA experienced stroke or death within 30 days after surgery. The incidence of stroke/death within 30 days increased with age, reaching 1.2% (n=28) for all patients 75 to 80 years and 2.2% (n=55) for all patients aged >80 years. Combined 30-day stroke/death rates were also significantly higher in those with life-limiting conditions as compared with those without life-limiting conditions (2.9% versus 1.1%, P<0.001). The incidence of stroke and death at 30 days was also higher among patients with life-limiting conditions as compared with those without life-limiting conditions (stroke: 1.8% versus 0.9%, P<0.001; death: 1.4% versus 0.3%, P<0.001; Figure 2).

In crude (unadjusted) analyses, the odds of mortality were nearly 5 times higher in asymptomatic patients with life-limiting conditions (OR, 4.6; 95% CI, 2.8–7.4; P<0.001). After adjustment for other baseline comorbidities, the presence of a life-limiting condition remained independently associated with 30-day stroke/death (OR, 2.8; 95% CI, 2.1–3.8; P<0.001; online-only Data Supplement II).

Overall, <1% of asymptomatic patients undergoing CEA experienced postoperative myocardial infarction (n=73). Although patients with life-limiting conditions experienced a higher incidence of postoperative myocardial infarction than
those without life-limiting conditions (0.8% versus 0.5%), this difference was not statistically significant ($P=0.06$).

**Effect of ASA Class IV and Severe COPD on Stroke and Death**

Because 2 of the most common life-limiting conditions in our cohort, ASA Class IV and severe COPD, were also the most subjective, we examined the effect of these variables independently on risk of stroke/death at 30 days. Compared with patients without life-limiting conditions, patients designated as ASA Class IV or with severe COPD had a higher incidence of stroke/death (2.9% versus 1.1%, $P<0.001$). Furthermore, the risk of stroke/death was even higher in patients with life-limiting conditions other than ASA Class IV or severe COPD (3.4%; Figure 3).

**Effect of Surgeon Specialty and Hospital Teaching Status**

When we examined the effect of surgeon specialty on outcome, we found that each surgical specialty examined performed approximately 20% of CEAs in patients with life-limiting conditions (19.9% vascular versus 21.0% other specialties combined, $P=0.497$). Furthermore, hospital teaching status was not associated with the proportion of CEAs performed in asymptomatic patients with life-limiting conditions (20.5% nonteaching versus 19.6% teaching, $P=0.205$).

**Comparison of Findings in Asymptomatic Versus Symptomatic Patients**

Lastly, to provide context for our results, we examined the prevalence of life-limiting conditions in patients undergoing CEA for symptomatic carotid stenosis, defined as CEA performed with a preoperative diagnosis of stroke or TIA. Overall, 27.1% (2731) of CEAs performed for symptomatic carotid stenosis occurred in patients with life-limiting conditions. Like with asymptomatic status, the most common life-limiting conditions in symptomatic patients undergoing CEA were ASA Class IV designation (16.0% of all symptomatic patients undergoing CEA) and severe COPD (10.9% of all symptomatic patients undergoing CEA). As expected, symptomatic patients had significantly higher rates of stroke and death than asymptomatic patients (stroke: 2.3% versus 1.1%, $P<0.001$; death: 1.0% versus 0.5%, $P<0.001$). Among symptomatic patients, those with life-limiting conditions experienced significantly higher rates of death and stroke/death at 30 days than those without life-limiting conditions (death: 2.0% versus 0.7%, $P<0.001$; stroke/death: 4.3% versus 2.6%, $P<0.001$). The incidence of postoperative stroke was also higher among symptomatic patients with life-limiting conditions, although this difference was not statistically significant (2.8% versus 2.2%, $P=0.095$; Figure 4).

**Discussion**

Our study demonstrates that among hospitals participating in a national surgical quality improvement program, CEA is performed commonly in asymptomatic patients with life-limiting conditions, and these patients have poorer perioperative outcomes. Furthermore, the cumulative effect of increased perioperative mortality, coupled with poor predicted 5-year survival as a result of having a life-limiting condition, makes it unlikely these patients will benefit, on average, from CEA for asymptomatic disease. Therefore, future efforts to examine the long-term benefit of CEA in patients with

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**Figure 2.** Thirty-day stroke, death, and combined stroke/death rates between patients with (black) and without (gray) life-limiting conditions after carotid endarterectomy for asymptomatic stenosis.
life-limiting conditions are necessary, especially in the current era of cost containment in health care.

After the Asymptomatic Carotid Atherosclerosis Study (ACAS) established the benefit of CEA for asymptomatic patients in 1995, many have examined the appropriateness of this procedure across a spectrum of patient risk. For example, in 1997, Cronenwett et al.18 published a cost-effectiveness analysis of CEA for asymptomatic patients based on trial data from ACAS. This study, which demonstrated an exponential increase in risk with increasing age >70 years, attributed the low net benefit of CEA in patients over this age threshold to a decreased life expectancy and therefore a reduced opportunity for stroke prevention. Other studies have also described populations that fare poorly in obtaining benefit from carotid endarterectomy, including the very elderly, blacks, and patients with chronic renal insufficiency.19–22

Our study finds that a significant proportion of asymptomatic patients selected for CEA in real-world practice are unlikely to experience durable long-term benefit from surgery. Although indirect, our data suggest that patients with life-limiting conditions have both increased perioperative mortality (1.4%) and increased predicted long-term mortality. These 2 elements make it unlikely that patients with life-limiting conditions will achieve the 3- to 5-year survival necessary to experience the benefit of stroke prevention provided by CEA for asymptomatic carotid stenosis.

Furthermore, in the present day, many argue that significant changes in the medical management of patients with asymptomatic carotid stenosis have occurred since ACAS was published. Specifically, rates of antiplatelet agent and statin use have increased,23 leading many to question whether CEA for asymptomatic patients still offers the same margin of benefit over nonoperative treatment. For example, Abbott24 published a meta-analysis describing a 7% decline in stroke and TIA in patients with severe carotid stenosis since the mid-1980s with the rate of ipsilateral stroke among medically treated patients falling below that of patients who received CEA in ACAS beginning in 2001. Given the uncertainty about the current effectiveness of CEA for asymptomatic carotid stenosis, many agree that a clinical trial is needed to compare newer methods of medical management for asymptomatic carotid stenosis with carotid revascularization across a spectrum of patient risk.

Practice patterns in patients with symptomatic carotid stenosis were not strikingly different than patients with asymptomatic stenosis in terms of the proportion of patients...
undergoing CEA in the setting of life-limiting comorbidities. However, the implication of a life-limiting condition is arguably much less important in patients with symptomatic carotid stenosis given their much higher potential risk of stroke in the near term. It is critical that patients undergoing surgery for asymptomatic carotid stenosis survive long enough to offset the upfront risk of surgery, whereas long-term survival is a less important parameter in determining the absolute benefit of CEA in patients with symptomatic carotid stenosis.

Our study has several limitations. First, we designated asymptomatic status based on the absence of a concomitant diagnosis of stroke or TIA not accounting for other potential symptoms not recorded in NSQIP such as ocular TIAs or dizziness. However, the proportion of CEAs we designated as asymptomatic in NSQIP is very similar to that of other regional registries and is likely representative of significant symptomatic status. A second limitation relates to our use of medical literature to infer the mortality rates associated with conditions defined in NSQIP. We recognize that the operational definitions available in NSQIP may not precisely align with definitions used in each of the outside sources cited. However, for 2 reasons, we believe our designations accurately represent life-limiting conditions. First, the studies we used to estimate mortality rates from life-limiting conditions were of high quality, including data from major randomized trials and federally supported registries. Second, the magnitude of differences in outcomes such as mortality and stroke observed between those with and without life-limiting conditions suggests that our designation of these conditions as life-limiting was likely accurate. A third limitation pertains to the diagnosis of postoperative stroke. Unfortunately, NSQIP does not require postoperative neurological examinations by personnel certified in the National Institutes of Health Stroke Scale and, as such, the diagnosis of this postoperative complication may vary from provider to provider. Fourth, our study is limited in the insight provided toward another important end point for patients undergoing carotid revascularization, myocardial infarction. Most clinical trials studying carotid revascularization use a broad definition, encompassing troponinemia, non-ST elevation myocardial infarctions, and ST-elevation myocardial infarctions. We found a low myocardial infarction rate in our study (1%), but likely because NSQIP uses a strict definition encompassing the most advanced manifestations of myocardial ischemia. Finally, some may question our selection of any 1 of our individual life-limiting comorbidities, especially variables indicative of overall patient risk such as ASA class designation. However, the magnitude of the survival differences in the characteristics we selected implies that we succeeded in identifying a cohort of patients for whom prophylactic surgery incurs very high risk.

**Summary**

Data from NSQIP suggest that approximately 20% of CEAs among asymptomatic patients are performed in patients with...
life-limiting conditions, who may not survive to realize the small but measurable long-term benefit of surgery for stroke prevention. Additionally, these patients have significantly higher rates of postoperative stroke and death than patients without life-limiting conditions, further increasing the chance that they will not benefit from CEA. Although current literature to guide surgeons in identifying patients at high risk for postoperative complications exists,26 these guidelines make little mention of patient selection for asymptomatic CEA based on long-term survival. Future efforts to examine actual (rather than predicted) rates of long-term stroke-free survival in patients with asymptomatic carotid stenosis and limited life expectancy are necessary.

Acknowledgments
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Disclosures
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References

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Key Words: carotid endarterectomy, asymptomatic, life expectancy, appropriate

Subject Codes: 13 (cerebrovascular disease/stroke); 49 (carotid stenosis); 76 (carotid endarterectomy)

Word Count: 4,116
S1. Conditions associated with limited life-expectancy and the associated operational definitions.

<table>
<thead>
<tr>
<th>Life-Limiting Condition</th>
<th>Operational Definition</th>
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<tbody>
<tr>
<td>Age ≥ 90 years</td>
<td>Do Not Resuscitate (DNR)</td>
</tr>
<tr>
<td>ASA Class IV</td>
<td>Patient has a physician signed DNR order in medical record</td>
</tr>
<tr>
<td>Severe COPD</td>
<td>Patient has a severe systemic disease that is considered a constant threat to life.</td>
</tr>
<tr>
<td>Severe COPD</td>
<td>Patient has both a diagnosis of COPD associated with one of the following: functional disability, hospitalization for COPD, requires chronic bronchodilator therapy, FEV1 &lt; 75% predicted.</td>
</tr>
<tr>
<td>Symptomatic CHF</td>
<td>Newly diagnosed CHF (within 30 days of surgery) or a diagnosis of chronic CHF with new symptoms/sign (within 30 days). Symptoms/Signs include: abnormal limitation in exercise tolerance due to dyspnea or fatigue, orthopnea, PND, increased JVP, pulmonary rales on exam, cardiomegaly</td>
</tr>
<tr>
<td>Advanced Liver Disease</td>
<td>Patient has ascites (presence of fluid accumulation in peritoneal cavity noted on physical exam, ultrasound or CT/MRI within 30 days of surgery) or esophageal varices (documented by EGD or CT within 6 months of surgery)</td>
</tr>
<tr>
<td>Dialysis Dependence</td>
<td>Acute or chronic renal failure requiring treatment with peritoneal dialysis, hemodialysis, hemofiltration, hemodiafiltration or ultrafiltration within 2 weeks prior to surgery</td>
</tr>
<tr>
<td>Disseminated Cancer</td>
<td>Patients with a diagnosis of cancer and one of the following: spread to ≥ 1 site in addition to primary, multiple metastases to indicate the cancer is widespread, fulminant or near terminal. The following are considered disseminated: ALL, AML, Stage IV lymphomas. The following are not considered disseminated: CLL, CML, Stage III lymphomas, MM.</td>
</tr>
</tbody>
</table>

ASA: America Society of Anesthesiology; COPD: chronic obstructive pulmonary disease; FEV1: forced expiratory volume in one second; CHF: congestive heart failure; PND: paroxysmal nocturnal dyspnea; JVP: jugular venous pressure; CT: computed tomography scan; MRI: magnetic resonance imaging; EGD: esophagogastroduodenoscopy; ALL: acute lymphocytic leukemia; AML: acute myelogenous leukemia; CLL: chronic lymphocytic leukemia; CML: chronic myelogenous leukemia; MM: multiple myeloma.
S2. Multivariate model for 30-day stroke/death following carotid endarterectomy for asymptomatic carotid stenosis

<table>
<thead>
<tr>
<th>Covariate</th>
<th>OR</th>
<th>95% CI</th>
<th>P-Value</th>
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<td>Life Limiting Condition</td>
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<td>2.1-3.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male Gender</td>
<td>1.1</td>
<td>0.8-1.4</td>
<td>NS</td>
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<tr>
<td>Diabetes</td>
<td>1.1</td>
<td>0.9-1.3</td>
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<td>Coronary Artery Disease</td>
<td>0.9</td>
<td>0.7-1.2</td>
<td>NS</td>
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<tr>
<td>Hypertension</td>
<td>1.1</td>
<td>0.7-1.7</td>
<td>NS</td>
</tr>
<tr>
<td>Smoker</td>
<td>1.0</td>
<td>0.7-1.4</td>
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