Housecalls
Underwriting Case Studies & Insights

September 2014 Vol. 6 #1

Solem® – New and Improved

There’s a joke in the industry: If you ask a life insurance specialist what one plus one equals, the answer will depend on whom you ask. The insurance accountant will confidently reply, “Two!” The actuary will pause and say “Well, that depends…” Meanwhile the underwriter will quickly answer, “Three!” We have achieved a “Three” by creating Solem Americas from two separate underwriting manuals.

Better Access, Currency and Content Relevance

As users become acquainted with the new underwriting manual (under SCOR’s Solem brand), several features should become evident quickly.

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<tr>
<th>User Friendly</th>
<th>Improved search functions</th>
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<td></td>
<td>Consistent format</td>
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<td>Related information</td>
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<th>Enhanced Financial Chapter</th>
<th>Both Canadian and US</th>
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<td>Reinforces the Americas</td>
<td>Used by all SCOR Global Life operations in the Americas</td>
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<td>Mortality ratings for US, Canada</td>
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<tr>
<th>Competitive Ratings</th>
<th>Provided opportunity to review rationale behind ratings for each major impairment</th>
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<td>Based on our greatly expanded medical and non-medical database</td>
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<th>Global Effort</th>
<th>Branded to reflect SCOR Solem brand</th>
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<td></td>
<td>Valuable input from across SCOR Global Life</td>
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A Refreshed Look and Feel

While content is of paramount importance, the delivery of that information must be intuitive and easy to follow. We examined the underlying technology and user appearance of both manuals with a goal of creating a system that is both readable for the user and flexible enough to be revised as needs arise.

To learn more about the content and functionality of our new manual please contact either your account executive or me. We are excited to share the new underwriting manual with you and look forward to your feedback.

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Vice President & Chief Medical Officer

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Vice President, Medical Director
Our Casebook
By Richard Braun, MD

Dr. Braun is Vice President & Chief Medical Officer for SCOR Global Life Americas. He received a Bachelor of Science Degree from the Towson State University (1975) and earned his Medical Degree from the University of Maryland (1979). Dr. Braun is board certified in Internal Medicine, Insurance Medicine and is a past President of the American Academy of Insurance Medicine.

Case #1 & 2 – Prostate Cancer and the PCA3 Test

Case #1
A 41 year-old man applied for life insurance. He had a family history of prostate cancer in his father, uncle and grandfather, and was being followed by a urologist. One year prior to the application his PSA was 4.8ng/ml. He was treated with an antibiotic and a repeat PSA was 3.3 ng/ml with a free PSA of 24%. At that time his digital rectal exam (DRE) revealed a prostate that was “2+ enlarged” without palpable nodule. A PCA3 test was done on the urine, with a Score of 13.1 (> 35 Abnormal). PSA at the time of application was 2.72.

Case #2
A 59 year-old man applied for life insurance. He was followed by a urologist for rising PSA. Three years before application his PSA was 1.9ng/ml. The PSA registered the same two years prior to application. The year before applying for life insurance, the PSA had risen to 3.9ng/ml, and 3 months prior to application it decreased slightly, to 3.4 ng/ml. The urologist performed a PCA3 test at the last visit, which scored 74. His DRE had always shown mild to moderate enlargement without nodule.

Question: What is the PCA3 Test or Score, and how does it affect the likelihood of prostate cancer?
Answer: In 1999 the PCA3 gene (Prostate Cancer Antigen 3) was described in prostate cancer specimens as being highly over-expressed. It was not found to be over-expressed in normal or hypertrophied prostate tissue. Tests were developed to measure the messenger RNA (mRNA) from the over-expressed gene in the urine. Typically the urine is collected after a described DRE that includes pressure from base to apex of the prostate. The result is most often given as a Score calculated from the PCA3 mRNA/PSA mRNA X 1000.

The use of PCA3 Score in the decision to perform a prostate biopsy is somewhat controversial because evidence to confirm the utility is still being gathered. At least one review, published in 2013, concluded that “PCA3 had a higher diagnostic accuracy than total prostate specific...”

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Figure 1 – Performance Characteristics of the PROGENSA PCA3 Assay Relative to Prostatic Biopsy Outcome (PCA3 Score ≤ 25)

<table>
<thead>
<tr>
<th>Performance Characteristics</th>
<th>Estimate</th>
<th>95% CI</th>
</tr>
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<tbody>
<tr>
<td>Sensitivity %</td>
<td>77.5 (%92/102)</td>
<td>68.4-84.5</td>
</tr>
<tr>
<td>Specificity %</td>
<td>57.1 (208/364)</td>
<td>52.0-62.1</td>
</tr>
<tr>
<td>PPV%</td>
<td>33.6 (79/235)</td>
<td>30.0-37.2</td>
</tr>
<tr>
<td>NPV%</td>
<td>90.0 (208/231)</td>
<td>86.5-93.1</td>
</tr>
<tr>
<td>PLR</td>
<td>1.81</td>
<td>1.53-2.11</td>
</tr>
<tr>
<td>NLR</td>
<td>0.40</td>
<td>0.26-0.56</td>
</tr>
<tr>
<td>Odds Ratio</td>
<td>4.58</td>
<td>2.75-7.62</td>
</tr>
</tbody>
</table>

CI = Confidence Interval, PPV = Positive Predictive Value, NPV = Negative Predictive Value, PLR = Positive Likelihood Ratio, NLR = Negative Likelihood Ratio

While not perfect, the PCA3 test appears to be a good predictor of prostate cancer with a score cutoff of 25. A PCA3 score of more than 25 is more closely associated with positive biopsies, whereas a score of 25 or less is more predictive of negative biopsy results.
antigen increases, but strength of evidence was low (limited confidence in effect estimates). Strength of evidence was insufficient to conclude that PCA3 testing leads to improved health outcomes. For all other outcomes and comparators, strength of evidence was insufficient.”

However, as our cases illustrate, the PCA3 test is available commercially and some clinicians are using it mainly to try to reduce the number of unnecessary prostate biopsies.

There appear to be 2 situations where PCA3 may be used clinically. The first is in the setting of a rising or elevated PSA where an initial biopsy is being contemplated. The PCA3 also may be an option after one or more negative biopsies, when the PSA remains elevated and further biopsies are being considered. Characteristics of the PCA3 test that would influence the biopsy decision are the sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV).

A review of the Physician Brochure for the PROGENSA PCA3 Assay reveals a recommended cutoff PCA score of 25 for clinical decisions. Figure 1 is taken from the brochure and contains the characteristics of the test.

A recent meta-analysis of 11 articles (3373 subjects) addressed the characteristics of the PCA3 test in the setting of repeat biopsy after the first was negative. The researchers analyzed the data using a PCA3 Score cutoff of <20 and of <35. The averaged results for the 11 studies are summarized in Figure 2.

While far from a perfect test, the table confirms that the lower the PCA3 Score value, the less likely that prostate cancer will be detected on biopsy. Some studies have indicated that PCA3 Scores “were significantly lower in low-volume disease and insignificant prostate cancer.” Another study in 2011 concluded: “PCA3 score may be a useful marker to improve the selection for Active Surveillance (AS) in addition to the current AS criteria. With a predictive cut-off of 25, PCA3...
score is strongly indicative for tumour volume and insignificant PCA.”

Figure 3 (previous page) also appears in the Physician Brochure for the PROGENSA PCA3 Assay. It details multiple findings related to prostate cancer risk and gives an indication of the relative importance of the risks (the higher the Odds Ratio, the stronger the indicator for risk). PCA3 appears to be a strong indicator of risk based on this small number of patients.

**Returning to the Cases**

**Case 1** exhibits a falling PSA and a low PCA3 score. It is less likely that prostate cancer is currently present. With a strong family history, continued monitoring will be important. A small excess mortality risk should be considered.

**Case 2** exhibits a rising PSA velocity and a markedly elevated PCA3 Score. This indicates excess risk of prostate cancer, which may be of larger volume. It would be prudent to await further investigation or follow-up to better delineate the extent of this risk.

**References:**


By William Rooney, MD, FAAFP, EMBA

Dr. William (Bill) Rooney is Vice President, Medical Director at SCOR Global Life Americas. Dr. Rooney’s responsibilities include facultative case review work, researching and updating Solem, researching and writing articles for a variety of SCOR publications and more. He earned a Medical Degree from the University of Missouri – KC (1981) & an Executive Master’s in Business Administration from Benedictine College in Atchison, Kansas (2009). He is board certified in Family Medicine with the American Board of Family Medicine.

**Case #3 – Vertebral Artery Dissection**

A 57 year-old male is applying for $1 million of life insurance. He has a remote history of a vertebral artery dissection occurring 7 years ago (at age 50). He evidently had an acute respiratory infection immediately before the acute onset of head and neck pain, which was quite sudden and severe. He also had just received a chiropractor adjustment for some neck pain, which had been an ongoing concern for several months. This onset of pain led to an ER visit.
MRA imaging revealed a dissecting left vertebral artery. Lumbar puncture was done and there was no sign of a subarachnoid hemorrhage. The hospital course was uneventful with no significant neurological deficit. Anticoagulation was started without complications.

Repeat imaging at 6 months to reassess vascular status revealed that complete revascularization had occurred. Clinical evaluation for evidence of any connective tissue disease was mentioned as being negative. Since this event the applicant has reported no recurrent problems and has had no further evaluation. Records document that he remains on a baby aspirin daily and avoids any neck manipulation or any sports involving sudden or excessive neck motion.

Questions

2 major questions arise when evaluating a case like this for mortality risk.

1. What is the risk of recurrence of arterial dissection in an individual with a previous history of extracranial vertebral artery dissection?

2. What is the long term mortality risk involved in an individual with vertebral artery dissection?

Answer: First, let's briefly review a few facts about extra-cranial vertebral artery dissection. Arterial dissection is a tear between the layers of the inside wall of an artery. A false lumen can develop as blood accumulates in the small pouch within the artery. This may lead to a stroke from the development of a thrombus and emboli from the thrombus traveling to and blocking small vessels in the brain. Alternatively, a thrombus may totally occlude the vessel, resulting in decreased blood flow and an ischemic stroke. Or, if the dissection ruptures through the blood vessel, bleeding into the brain (subarachnoid hemorrhage) may result in a cerebrovascular accident.

Possible causes of arterial dissection include a hereditary predisposition, which can involve a connective tissue disorder (e.g., Ehlers-Danlos syndrome type IV and Marfan syndrome) or vascular conditions (fibromuscular dysplasia). However, this is a relatively rare cause for the condition (probably less than two percent caused by Ehlers-Danlos syndrome, for instance). Figure 2 lists many of the connective tissue and vascular disorders associated with dissection.

More commonly the dissection will follow physical trauma with forceful neck movements, such as basketball, swimming, scuba diving, skating, roller coaster rides, automobile accidents, or even coughing or sneezing. Population controlled studies have shown an association between chiropractor neck manipulation and vertebral artery dissections. Hair washing at beauty parlors, recent infections as well as elevated homocysteine levels also have been postulated to play a role.

Arterial dissection can occur in the carotid artery as well as the vertebral artery. One study showed the incidence of spontaneous internal carotid artery dissection to be 1.72 per 100,000 individuals compared to vertebral artery dissection of 0.97 per 100,000 individuals. Most authorities evaluate and treat internal carotid artery dissection similarly to vertebral artery dissection, classifying them as either extra-cranial artery or intracranial artery dissection. The CADISP study involving 982 patients generated interesting results (Figure 3, next page).

Regardless of the etiology, vertebral artery dissection and carotid artery dissection account for up to 20% of cases of stroke in young adults. Dissection
Neck pain and HA are most closely associated with dissection, according to the CADISP study of 982 patients.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Vertebral Dissection</th>
<th>Internal Carotid Dissection</th>
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<tbody>
<tr>
<td>Bilateral dissection</td>
<td>16%</td>
<td>10%</td>
</tr>
<tr>
<td>Associated with minor trauma</td>
<td>37%</td>
<td>29%</td>
</tr>
<tr>
<td>Neck Pain at presentation</td>
<td>66%</td>
<td>39%</td>
</tr>
<tr>
<td>Associated with recent infection</td>
<td>15%</td>
<td>22%</td>
</tr>
<tr>
<td>Mean age</td>
<td>41</td>
<td>46</td>
</tr>
<tr>
<td>Transient monocular blindness</td>
<td>0</td>
<td>8%</td>
</tr>
<tr>
<td>HA at presentation</td>
<td>65%</td>
<td>68%</td>
</tr>
</tbody>
</table>

Neck pain and HA are most closely associated with dissection, according to the CADISP study of 982 patients.

Most often results in an ischemic stroke or transient ischemic stroke. 60-90% of cases have a symptom of head and/or neck pain. Up to 20% will have sudden and severe onset of this pain. Other symptoms include tinnitus, vertigo, orbital pain, or cervical nerve root complications.

Diagnosis is typically made by neuroimaging. An angiogram, MRA or CTA are common diagnostic procedures which will help establish the diagnosis. The MRA and CTA are frequently done to avoid the more invasive angiogram. The sensitivity and specificity of the MRA is similar to the CTA. Lumbar puncture is frequently done if there is concern about the presence of an associated subarachnoid hemorrhage.

Treatment typically includes antithrombotic therapy with either anticoagulation or antiplatelet medications. Some clinicians prefer anticoagulation for small or moderate sized infarction in the setting of an extra-cranial dissection, and antiplatelet therapy for larger infarcts. The presence of a subarachnoid hemorrhage generally discourages the use of anticoagulation however. Some clinicians prefer antiplatelet therapy for those with dissection and non-ischemic symptoms.

Unfortunately there is a paucity of controlled studies directly comparing treatment modalities, combinations of treatments, and length of treatments. Guidelines issued by the American Heart Association/American Stroke Association (AHA/ASA) in 2011 do suggest antithrombotic therapy for at least three to six months as reasonable. The 2012 American College of Chest Physicians (ACCP) guidelines suggest using the general recommendations for patients with non-cardioembolic stroke, which typically involves aspirin initially and antiplatelet therapy (e.g., aspirin, clopidogrel, or cilostazol) for secondary prevention.

The 2011 ASA/ASA guidelines suggest considering endovascular therapy with stenting for those who fail adequate antithrombotic therapy and consider surgery for those who fail stenting.

The prognosis for vertebral artery dissection, as is true generally for other types of strokes, is related to the severity of the associated ischemic stroke and/or subarachnoid hemorrhage. Better outcomes are associated with lesser initial stroke severity and those cases which show recanalization.

One study published in *Stroke* in 2006 evaluated outcomes in 169 patients with spontaneous vertebral artery dissection (SVAD). Brain ischemia occurred in 131 patients (77%; ischemic stroke 67% TIA 10%). Six (4%) suffered subarachnoid hemorrhage. Two patients died (2%) at 3 months. Many feel that factors associated with poor functional outcome include a high NIHSS score at onset, arterial occlusion, and older age. Half of long-term survivors suffer from significant quality-of-life impairments.

Recanalization results have varied by study and observed timeframe. One study reported complete recanalization of the vertebral artery at six months in 62% of the 61 patients with dissection. In another study, 51% of the 76 patients with cervical artery dissection had complete recanalization at nine months and another 20 percent had partial recanalization.

Recurrence of cervical artery dissection...
does occur at times but the literature is somewhat inconsistent in the magnitude of this risk. Retrospective studies have suggested an approximate risk of 1% annually. However, in the CADISP study mentioned earlier the recurrence rate at 3 months was 2%. The rate in other studies ranges from 0-13%.

In summary, patients that experience an extra-cranial dissection have excellent or complete short-term recovery in 70-85% of cases, death in approximately 5% of cases, and disabling complications in 10-25% of cases. Mortality may be higher in those with intracranial dissection. Long-term mortality data is lacking but current data suggest recurrence of ischemic stroke is in the 0-13% range. The presence of an underlying connective tissue disease, vascular disease, or hereditary condition predisposing to this condition would increase the risk of recurrence. Documentation of adherence to follow-up evaluation and therapeutic recommendations, complete revascularization of the artery on repeat neuroimaging, and the lack of residual neurological deficits would be favorable prognostic characteristics.

**Returning to the Case**
In this particular case, an underwriter assessing future mortality risk should note several favorable factors. The history of a unilateral vertebral artery dissection without significant neurological deficit and with no evidence of recurrence is encouraging. Likewise, complete revascularization revealed in repeat imaging of the artery is promising. Finally, there is documentation that there are no findings of any underlying condition which would make recurrence more probable. The respiratory infection and the neck manipulation preceding the dissection may indicate a traumatic cause. He is actively trying to mitigate risk of future events. Seven years have passed without recurrence. There appears to be minimal risk of recurrent dissection in this particular case.

**References**


Biller, Jose, et al. “Cervical Arterial Dissections and Association With Cervical Manipulative Therapy.” *Stroke.* Published online 8-7-2014.


Underwriting Puzzler...
By William Rooney, MD, FAAFP, EMBA

In this issue of the Puzzler Dr. Rooney presents another EKG. What is the major abnormality in the following EKG? Do you see any other irregularities that warrant further analysis?

To find the answer, be sure to visit the Housecalls page on www.scorgloballifeamericas.com. Click on the “September Puzzler” Powerpoint presentation to confirm your findings.

For More Information...

SCOR has a number of valuable studies and papers related to medical and underwriting issues available on its website, at www.scor.com/en/skor-global-life/life-publications.html.

Publications are tabbed by newsletter title under the “Life publications” title.