Proposal for RO1 – Translating Research Into Practice

Project Title:
Diagnosis of Proximal Deep Vein Thrombosis of the Lower Extremity in Outpatients Following Hip or Knee Surgery: A Cluster Randomized Trial

Background:
Deep vein thrombosis (DVT) and pulmonary embolism, a common sequela of DVT, is an important public health problem that is reported to be responsible for approximately 500,000 deaths in industrialized countries each year. Orthopedic surgeons frequently assess outpatients with orthopedic problems for the presence of proximal deep vein thrombosis (PDVT) of lower extremity. No research has reported whether orthopedic surgeons correctly diagnose outpatients with PDVT. Given that PDVT is a relatively common condition, misdiagnosis or late diagnosis of this condition likely results in substantial mortality and morbidity.

PDVT is reported to be the most commonly seen complication following hip or knee arthroplasty and traumatic orthopedic injuries. In many cases, PDVT does not appear until after a patient has been discharged from the hospital and is being treated as an outpatient. PDVT associated with in hospital care for orthopedic patients is well recognized but PDVT associated with outpatient or post hospital care is less frequently discussed and may be under-recognized. If outpatients with PDVT can be identified early, the risk for severe morbidity and mortality can be lessened. Recently published evidence indicates that use of a clinical decision rule (CDR) in combination with non-invasive diagnostic testing is the most effective approach for identifying patients with this potentially fatal condition. The primary aim of this study is to establish whether an evidence-based intervention designed to train orthopedic surgeons to diagnose PDVT using methods supported by current evidence results in a patients being diagnosed with PDVT significantly earlier as compared to usual care.

Preliminary investigations:
We recently completed an Agency for Healthcare Research and Quality funded RO3 (HS13059-01) designed, in part, to determine if orthopedic surgeons can accurately estimate the probability of PDVT. We used a series of clinical vignettes imbedded in a survey and the survey was sent to a random selection of 2300 orthopedic surgeons in the US. The gold standard measure of the likelihood of PDVT in each scenario was modeled after the validated CDR of Wells et al. The CDR classifies patient risk of PDVT as low (<5%), moderate (~17%) or high (~50%). A total of 676 (31%) surgeons completed the survey. With the exception of an under-representation of female orthopedists, we found no evidence of non-response bias or sample bias. For the two high probability vignettes, 53% and 84% of orthopedists under-estimated probability. For the two low probability vignettes, 43% and 75% of orthopedists over-estimated the probability of PDVT. In multivariate analyses, orthopedist age, board certification status, practice type and region of the country did not explain the findings. For all but one scenario, at least 80% of the surgeons indicated that they would have ordered diagnostic tests. For the low probability cases, <1% of the surgeons would have requested a D-dimer, a commonly advocated test in the general medical literature. For moderate and high probability cases, at least 80% of surgeons would have requested ultrasonography, the test most commonly advocated for these types of cases. For the moderate and high probability cases, 20% to 41% of respondents would do a repeat ultrasonography if the first test was negative. Evidence supports the use of repeated ultrasounds on patients with moderate or high probability to be confident that PDVT has been ruled out.
Table 1 summarizes the probability estimates and Table 2 summarizes the proportion of surgeons recommending the appropriate evidence-based diagnostic test for each vignette.

Table 1 – For each scenario the number of orthopedic surgeons who estimated the probability as low, moderate or high is reported. The bars indicate the proportion classifying patient risk as low, moderate or high for each scenario. The two low probability scenarios are on the left, the two moderate probability scenarios are in the middle and the two high probability scenarios are on the right.

Table 2 – Summary of the proportion of surgeons who would prescribe the correct diagnostic test for each scenario. For the low probability cases, D-dimer is the appropriate test and for the moderate and high probability scenarios, ultrasound is the appropriate test. The raw numbers in the tables represent estimates extrapolated to the entire population.

We concluded that many orthopedists’ estimates of the probability of leg DVT in outpatients could be improved by use of Wells’ clinical decision rule. Diagnostic accuracy and efficiency
would likely also be enhanced by the use of targeted diagnostic testing (selective use of
diagnostic ultrasound and D-dimer blood tests) as recommended in the general medical literature.

**Primary Aims of the Proposed Study:**
The primary aim of the proposed study is to:

1) Determine if the time to diagnosis of DVT in outpatients is significantly less in the experimental group clinics as compared to the control group clinics.
   Hypothesis: Outpatients with DVT will be diagnosed significantly earlier in the experimental group as compared to the control group.

Secondary aims are the following:

1) Determine if use of evidence-based procedures for diagnosis of DVT results in a greater proportion of patients diagnosed with DVT as compared to control group clinics.
   Hypothesis: Clinics in the experimental group will use evidence-based diagnostic procedures to identify a significantly greater proportion of patients in their clinics who have DVT as compared to control group clinics.

2) Determine if a greater proportion of patients in the experimental group undergo diagnostic testing in accordance with published evidence as compared to patients in the control group.
   Hypothesis: A significantly greater proportion of at-risk patients in the experimental group will be tested in accordance with published evidence as compared to patients in the control group.

**The Intervention:**

Our preliminary plan is as follows. The three behaviors we hope to change are 1) clinicians’ use of the CDR developed by Wells et al and 2) clinicians’ use of diagnostic testing in accordance with published evidence. The interventions can be briefly summarized in the following figure. 3) patients’ prompt notification of the clinic when symptoms that may be associated with a DVT are perceived.

The CDR by Wells and colleagues is a validated clinical tool designed to estimate probability in patients suspected of having PDVT. A score of 0 or less indicates low probability (5.6%, 95% CI=3.5% to 8.7%), a score of 1 or 2 indicate moderate probability (14.1%, 95% CI=8.6% to 22.4%) and a score of 3 or higher indicates high probability (47.4%, 95% CI= 35.3% to 60%) (See table).
Table – Clinical Decision Rule Developed by Wells and Colleagues

<table>
<thead>
<tr>
<th>Clinical Finding</th>
<th>Score</th>
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<tbody>
<tr>
<td>Active Cancer (treatment or within 6 months or palliative)</td>
<td>1</td>
</tr>
<tr>
<td>Paralysis, paresis or recent plaster immobilization of lower extremity</td>
<td>1</td>
</tr>
<tr>
<td>Recently bedridden &gt;3 days or major surgery within 4 weeks</td>
<td>1</td>
</tr>
<tr>
<td>Localized tenderness along distribution of the deep venous system *</td>
<td>1</td>
</tr>
<tr>
<td>Entire leg swelling</td>
<td>1</td>
</tr>
<tr>
<td>Calf swelling by &gt;3 cm compared to asymptomatic leg #</td>
<td>1</td>
</tr>
<tr>
<td>Pitting edema (greater in the symptomatic leg)</td>
<td>1</td>
</tr>
<tr>
<td>Collateral superficial veins (non varicose)</td>
<td>1</td>
</tr>
<tr>
<td>Previously documented DVT</td>
<td>1</td>
</tr>
<tr>
<td>Alternative diagnosis as likely or greater than that of DVT ^</td>
<td>-2</td>
</tr>
</tbody>
</table>

The CDR combined with diagnostic tests is the current evidence-based approach to the diagnosis of PDVT. The algorithm illustrated in the figure is supported by extensive research evidence \(^{10,11}\) as well as recommendation in clinical guidelines \(^{12,13}\) and a recently published Evidence Report \(^{14}\).

Figure. Algorithm illustrating the application of the clinical decision rule and application of appropriate diagnostic tests given current evidence.
The intervention for the experimental group will consist of a video of an expert applying the CDR to an outpatient following a hip or knee surgery. The video will illustrate each procedure and will clearly demonstrate that the CDR is simple and takes approximately 2 minutes to complete. In addition, the video will demonstrate the use of the D-dimer test, a simple finger-stick blood test. The video will also discuss the role of diagnostic ultrasound in the diagnosis of PDVT. In summary, the video will discuss all aspects of the algorithm above and will be approximately 20 minutes in length. A copy of the video will be supplied to each surgeon and all support staff along with one copy for the clinic. In addition, the video will be placed on a web page for access on the web. The intervention will also include a reminder, posted on the patient chart, to each physician/nurse to complete the CDR on each patient. It is likely that the support staff (nurses and physician assistants will be the clinicians responsible for the screening procedures described above). The reminder will be the 1 page CDR checklist along with the score obtained on the checklist. The patients will also be given an educational handout and instruction by a nurse on the importance of prompt notification of the office should the patient develop symptoms suggesting the presence of DVT.

The control group will receive the summary evidence report from the AHRQ but will not receive any other formal training. The literature suggests that distribution of written materials has essentially no effect in changing physician behavior so this group will essentially be a control group.

Methods:
Because this will be a cluster randomized trial, clinics will be randomized to either the intervention or the control group. Because of the risk of contamination among individual surgeons, we will randomize at the level of the clinic. A research nurse will be recruited from each participating clinic. The research nurse will manage data collection in each clinic and will be contacted by the PI on a bi-weekly basis to monitor progress.

All patients who have a complaint of calf or thigh pain or swelling and who have had a recent (within 30 days) hip or knee surgery will be admitted to the study. Patients will be admitted in both arms during either their first or second postoperative visit or prior to surgery if the surgery is elective. Clinicians will complete the CDR on all patients in the experimental group. The clinician who will apply the checklist will be either a trained nurse, physician’s assistant, nurse practitioner or the surgeon. The clinician will be asked to make a judgment, after completion of the CDR, of whether he or she is suspicious of a PDVT. Some patients who meet the admission criteria will have symptoms of thigh or calf pain or swelling as a routine consequence of their surgery and in these cases the clinicians will indicate such and the patient will be followed for three months to determine if a PDVT or PE occurred. If the practitioner suspects a PDVT, the algorithm will be applied in the following way: If the patient is judged to have a low probability of PDVT, based on the CDR, the patient will have a D-dimer test done. If the D-dimer is negative then PDVT has been ruled out. If the D-dimer is positive, the patient will be referred for ultrasound. If the probability of PDVT is judged to be moderate or high, an ultrasound will be prescribed. If the initial ultrasound is negative then a follow-up ultrasound will be done approximately one week later.

Patients in the control group will receive “usual care.” Clinicians will be asked if they are suspicious of PDVT during the patient’s first or second postoperative visit. For patients in whom the clinician is not suspicious of PDVT the patient will be followed for three months as in the experimental group. For patients in whom the clinician is suspicious of PDVT, data will be collected on the number and type of diagnostic tests done and whether PDVT was diagnosed.
Data Analysis:
For cluster randomized trials, reliable estimates of intracluster correlation coefficients (ICC) are required for accurate estimates of sample size. Estimates for process variables (like the primary dependent variable to be used in this study) in the United Kingdom are on the order of .05 to .15. Currently we are aware of no evidence of the ICC for process measures like that proposed in this study for orthopedic surgeon practices in the US. To make an estimate of sample size, we will use an ICC of .10 until a better estimate can be generated. To find a mean difference of 10 days (sd=10) in the time to diagnosis between the experimental and control groups, a total of 5 clinics per arm are needed for the study. This sample size would provide us with an alpha of .05 and power of 80% to detect the stated differences in time to diagnosis. Evidence suggests that a 10 day improvement in the time to diagnosis will potentially reduce morbidity and mortality in patients who have a PDVT.