Appendix 1. Functional Status Measures

Background

Assessment of neurological recovery is an important component of evaluating the effects of resuscitation interventions. Neurological injury after cardiac arrest contributes to in-hospital death often because of withdrawal of care.[1] Some surviving patients have decrements in cognitive function,[2-4] although most surviving patients enjoy good quality of life.[5;6] Neurological status varies over time with large improvements during the first few days after resuscitation.[7;8] Detailed neuropsychiatric testing reveals that most improvement occurs during the first 3 months after resuscitation,[3;7] with only small clinical changes during rehabilitation in those with severe anoxic brain injury.[9;10] These studies suggest that it is possible to reliably measure neurological status three months after resuscitation. Criteria for choosing an instrument to measure neurological status include prior data about reliability and validity, availability of instruments suitable for a multicenter trial, and application to prior cardiac arrest survivors.

The **Modified Rankin Scale (MRS)** will be assessed from the clinical record prior to discharge and by telephone interview after discharge. It has face validity and can be determined in person or over the telephone. MRS has concurrent validity with other measures of neurological recovery after stroke and brain injury.[11;12] Use of a structured interview in a recent study of stroke patients improved the weighted kappa from 0.71 to 0.91[13]. The only previous published applications of MRS to survivors of cardiac arrest evaluated a cohort of neurosurgical patients with in-hospital cardiac arrest [14] and a cohort of survivors of out-of-hospital cardiac arrest.[4]

The Cerebral Performance Category (CPC) will be assessed from the clinical record prior to discharge and by telephone interview after discharge. Consensus statements recommend use of the CPC to assess functional outcomes after resuscitation from cardiac arrest.[15;16] CPC is a five-

point scale that was adapted from the Glasgow Outcome Scale.[17;18] CPC has limited discrimination between mild and moderate brain injury. A small study with incomplete follow-up of survivors demonstrated only moderate correlation with other measures of health-related quality of life.[19] However, CPC at discharge predicts long-term survival.[20]

An interesting question is whether simple MRS or CPC scores at discharge correlate with more detailed assessments post discharge. We primarily intend to apply the MRS and CPC at discharge and will apply more detailed measures once the patient has been contacted post discharge. A limitation to the post discharge assessment of MRS or CPC scores is that there is no well-validated 26 instrument for either measure. Also, proxy respondents tend to overestimate patient burden,[21] and may or may not be available for interview. Therefore, we shall assess MRS or CPC at discharge based on review of the clinical record, and after discharge based on interview at three and six months. MRS will be assessed after discharge by using an instrument validated for telephone administration.[13] CPC will be assessed by using a structured questionnaire via telephone administration. These latter questions were developed based on experience assessing outcomes after discharge in the OPALS study, PAD trial and ASPIRE trial as well as previous work by others to develop a structured phone interview to assess the related Glasgow Outcome Score.[22] However, it should be recognized that these questions have not been validated in their current format.

Generic health-related quality of life [23;24] will be measured three and six months after discharge by administering the **Health Utilities Index Mark 3 HUI system.**.[25] The interview-administered version of HUI3 requires completion of a maximum of 39 questions. (www.healthutilities.com accessed on October 14, 2005). The HUI3 consists of eight attributes of health (vision, hearing, speech, mobility, dexterity, emotion, cognition, and pain) with 5 or 6 levels per attribute. For each attribute, no, or mild, impairment in health has been defined as better than level 3 function (or

level 4 function in the cognitive attributes). For each respondent, health status is described as a vector that combines the levels of each attribute. The health status information is then converted into a utility score of health-related quality of life on a scale from perfect health (1.0) to death (0).[25;26] Shown to be reliable and valid in other populations.[27-29]. The HUI3 has been used in several ongoing studies of interventions for individuals with sudden cardiac arrest. [5;30] This health-related quality of life index is consistent with current standards for economic evaluation of health technologies.[31]

Neurological status will be measured at one, three and six months after discharge by using the **Adult Lifestyle and Function (ALFI) version of the Mini-Mental Status Exam (MMSE)**.[32;33] The ALFI-MMSE has 23 items. Our experience using it in the PAD trial suggests that it requires approximately five minutes to administer. It is scored from 0 to 22, with a cutoff of 16/17 used to determine cognitive impairment. ALFI-MMSE correlates strongly (Pearson's r 0.73 to 0.85) with face-to-face MMSE across all patients or when grouped by Clinical Dementia Rating Scale class.[33] Five items were discrepant ($p< 0.05$) between phone and face-to-face versions: day of the week, county, name of place, phrase repetition, and registration of the term "penny." Respondents were more likely to give incorrect answers face-to-face to the first three of these items, while repetition and registration of the item "penny" were significantly less accurate over the phone. Compared to the brief neuropsychiatric screening test, which is a weighted score of the Trailmaking A,[34] Word Fluency,[35] Weschler Memory Scale-Mental Control and Logical Memory,[36] ALFI-MMSE had a sensitivity of 68% and specificity of 100% for mild cognitive impairment. The corresponding MMSE values were 67% and 100%.

Finally, depression will be assessed three and six months after discharge by using the **Geriatric Depression Scale** administered by telephone (T-GDS)[37] since depression is observed in those with cardiovascular disease[38] or those who have survived cardiac arrest,[3] and can be difficult to

differentiate from cognitive impairment. This instrument has 30 items that are answered either 'yes' or 'no.' It is scored from 0 to 30, with a cutoff of 10/11 used to determine cognitive impairment.[39] T-GDS has moderate test-retest reliability during a one-week period (Kappa 0.35 to 0.7, mean 0.52) Using a cutoff of 10/11T-GDS has a sensitivity of 86% and specificity of 70% for detecting depression compared to a comprehensive assessment by a geriatric psychiatrist. Although initially designed to measure depression in older adults, it is also internally consistent and valid in younger adults.[40]

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Appendix 2. Monitoring of CPR Process

Rationale for Monitoring CPR Process

Recent studies have demonstrated that CPR is frequently not performed according to evidence-based guidelines in both the out-of-hospital and in-hospital settings.[1;2] Although these studies lacked power to detect a significant relationship between CPR performance and patient outcome, a related study demonstrated that a greater rate of chest compressions was associated with a greater likelihood of achieving ROSC.[3] The importance of monitoring and improving CPR performance was confirmed by the observation of potentially deleterious hyperventilation in the Milwaukee pilot study of ITD.[4]

Method of Monitoring CPR Process

All ROC clinical trial sites will implement a high-quality system for monitoring individual components of CPR; specifically, the rate of chest compressions, and the proportion of pulseless resuscitation time during which chest compressions are provided (i.e. CPR fraction), collectively referred to as CPR process. Recent studies show no significant differences in these parameters during the first five minutes of resuscitation as compared with the entire resuscitation episode.[1;2] It is anticipated that during the initial period, interruption of CPR due to rhythm analysis or other procedures is more likely than throughout the resuscitation episode. After insertion of an advanced airway and initiation of ventilation that is asynchronous with chest compressions, hyperventilation is more likely than during the early resuscitation period. Therefore, CPR process will be monitored for a minimum of the first analyzable five minutes in all resuscitations. In addition, CPR process will be monitored for a minimum

of five minutes after receipt of an advanced airway. Where feasible, sites will be encouraged to monitor CPR process for the entire resuscitation. Sites will be required to demonstrate an ability to adequately acquire and analyze these CPR process data, identify and attempt to correct any observed deficiencies, and meet minimum performance standards before being eligible to enroll patients in the present trial. In addition, ongoing monitoring and review of the CPR process will be used throughout the conduct of the trial.

At the completion of every resuscitation attempt, the electronic record from the BLS and ALS devices used during the call will be obtained. All electronic records will be reviewed manually by proprietary automated analysis software. Determination of whether a resuscitation effort meets minimally acceptable CPR performance standards for the ROC will be based on whether it meets acceptable chest compression rate, and CPR fraction criteria as defined in Table 3.

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