

Time-Limited Trials in End of Life Care

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Background

Time-limited trials are treatment plans and agreements between patients/decision makers and clinical teams to utilize medical therapies over a set time. Involved parties watch patients’ clinical statuses to determine a path to continue with the treatment versus shift towards more palliative measures. Here we discuss how time-limited trials can provide a framework for providing care near end of life.

Case Description

Patient was a 78-year-old man with notable past medical history of bipolar I disorder and chronic kidney disease stage III who presented with weakness, 30 pound weight loss over 4 months, altered mental status, and falls. His wife noted symptoms started after an inpatient psychiatric stay months prior for acute mania, where risperidone and valproic acid were started.

Physical exam –

- Febrile to Tmax >100.2, tachycardic to 110, and hypoxic to 82% requiring up to 5 L of oxygen.
- Masked facies, bradykinesia, resting tremor, cogwheel rigidity of upper extremities, shuffling gait, and anhedonia.
- Alert and oriented with periods of somnolence. At times drooling and aspirating with course breath sounds.

Pertinent laboratory studies/ imaging –

- Creatinine 1.9 (baseline ~1.5), potassium 3.0, phosphorus 2.2, albumin 3.3.
- White blood cell count 5, hemoglobin 9.
- Valproic acid level 87. UA noninfectious. TSH, B12, folate all normal.
- MRI brain with diffuse cerebral cortical atrophy.
- Chest X-ray with patchy bibasilar airspace disease, slightly increased at the left lung base.

Case Description (cont.):

It was suspected that patient had extrapyramidal symptoms and drug-induced parkinsonism driven by both medications in the context of impaired renal function. However, patient had ongoing dysphagia and failed swallow evaluations.

Nasogastric tube placed as the family felt the patient would agree with temporary feeds to monitor for improvement with ongoing goals of care discussions and psychiatric medication changes. The patient was lucid at times to discuss the treatment plan and his values and goals. They pursued percutaneous endoscopic gastrostomy (PEG) tube while weaning psychiatric medications for possible recovery, understanding PEG tubes would not decrease aspiration risk.

The patient declined and was unable to tolerate tube feeds, with large residuals and multiple aspiration events. He required frequent suctioning, multiple courses of antibiotics for aspiration pneumonia, and escalating oxygen needs. Team expressed to family that patient was unlikely to meaningfully recover with current medical therapies. Family felt that despite attempts and time for recovery, he would not want to continue in this current quality of life and decided to transition to comfort care and pursue inpatient hospice.

Table. The 5 Components of a Time-Limited Trial (TLT) and How They Map Onto the Clinical Experience of Patients

TLT: the 5 parts	Example 1 (from Quill and Holloway ³)	Example 2 (the present patient from the “Story From the Front Lines”)
Define acute clinical needs and prognosis	Acute hypoxic respiratory failure secondary to end-stage heart failure requiring invasive mechanical ventilation; the ability to breathe without the ventilator is dependent on the ability to diurese adequately	Hemorrhagic shock due to duodenal ulcer; immediate prognosis dependent on ability to achieve hemostasis and time to resolution of shock
Clarify goals and values of the patient	Liberation from mechanical ventilation	Wish to discharge to home with hospice and spend remaining time with family
Identify objective markers of clinical status	Ability to improve oxygen requirements with diuresis	Ability to wean vasopressors, identify intervenable bleeding source, and achieve transfusion goals
Identify time frame for re-evaluation	3 to 7 d, Depending on family and clinician discretion	Discuss clinical status at 24 and 48 h after admission, as well as likely trajectory after endoscopy
Define potential actions to be taken at end of TLT	Discuss that the goal is to discharge the patient to home if they can be liberated from the ventilator with diuresis; if unsuccessful, long-term mechanical ventilation is not recommended, and a transition to comfort-focused care may be most appropriate	Discuss that the patient will be discharged home if the bleeding can be stopped, but if unsuccessful, a transition to comfort-focused care may be most appropriate

Figure 1. Explanation of goals of time limited trials with examples. See reference No 3.

Conclusion

Time-limited trials can be included in the framework for goals of care discussions by identifying objective markers of clinical status and setting goalposts within set time frames. While no defined metrics had been set in this case, with each discussion regarding pursuing procedures and therapies, the family and patient were able to define goals and various clinical measures to determine improvement versus deterioration to inform the decision making.

By having these conversations, this allows all parties to better understand the benefits and burdens of medical treatment to then help align care with patient and family preference. This is vital in improving communication and potentially decreasing intensity and length of non-beneficial treatments.

Selected References

1. Quill TE, Holloway R. Time-Limited Trials Near the End of Life. *JAMA*. 2011;306(13):1483–1484. doi:10.1001/jama.2011.1413
2. Chang DW, Neville TH, Parrish J, et al. Evaluation of Time-Limited Trials Among Critically Ill Patients With Advanced Medical Illnesses and Reduction of Nonbeneficial ICU Treatments. *JAMA Intern Med*. 2021;181(6):786–794. doi:10.1001/jamainternmed.2021.1000
3. Popovich JJ, Budnick I, Neville TH. Time-Limited Trials of Intensive Care Unit Care. *JAMA Intern Med*. 2023;183(4):360–361. doi:10.1001/jamainternmed.2022.6792