

Supportive Care: Comprehensive Conservative Care in End-Stage Kidney Disease

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Abstract

Comprehensive conservative (nondialytic) kidney care is widely recognized and delivered but until recently, has not been clearly defined. We provide a clear definition of comprehensive conservative care. This includes interventions to delay progression of kidney disease and minimize complications as well as detailed communication, shared decision making, advance care planning, and psychological and family support. It does not include dialysis. Limited epidemiologic evidence from Australia and Canada indicates that, for every new person diagnosed with ESRD who receives dialysis or transplant, there is one new person who is managed conservatively (either actively or not). For older patients (those >75 or 80 years old) who have higher levels of comorbidity (such as diabetes and heart disease) and poorer functional status, the survival advantage of dialysis may be limited, and comprehensive conservative management may be considered; however, robust comparative evidence remains limited. Considerations of symptoms, quality of life, and hospital-free days are as or sometimes more important for patients and families than survival. There is some evidence that communication about possible conservative management options is generally insufficient, even where comprehensive conservative care pathways are already established. Symptom control and the cost-effectiveness of interventions are addressed in the companion papers within this Moving Points in Nephrology series. There is almost no evidence about which models of care and which interventions might be most beneficial in this population; future research on these areas is much needed. Meanwhile, consistency in definition of comprehensive conservative care and basing interventions on existing evidence about survival, symptoms, quality of life, and experience will maximize patient-centered and holistic care.

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Introduction

The purpose of this paper is to clarify the definition of conservative (nondialytic) care of ESRD and report the evidence on prevalence, survival, symptoms, quality of life, and illness experience in relation to conservative management. It also delineates the implications of this evidence for clinical care and research.

Defining Conservative Care

Conservative (nondialytic) kidney care is widely recognized and delivered, but until recently, it has not been clearly defined. The Renal Physicians Association Shared Decision-Making Guideline uses the term “active medical management without dialysis” (1,2). A range of alternative terms, such as conservative care, maximal conservative management, renal supportive care, palliative care, or supportive care, has been used in relation to nondialysis care in ESRD but without clear definition. This has constrained recognition of the health care needs of this sector of the ESRD population and prevented systematic study to build evidence on ways to best improve care and outcomes. The occasional use of the terms palliative care or supportive care as synonymous with nondialytic care is particularly misleading, because palliative and supportive care can be provided alongside dialysis as well as conservative care.

To counter this, a recent consensus conference (3) proposed a detailed, specific definition for conservative

care in ESRD, suggesting adoption of the term “comprehensive conservative care” to reflect the full extent of conservative management (3) and providing a full definition (Table 1) of what comprehensive conservative care should include. The conference also proposed three distinct groups within the conservative care population (Table 2) to address concerns about availability of RRT and options for choice across the spectrum of low-, middle-, and high-income countries.

How Common Is Conservative Care?

One of the first considerations is understanding the size of the population of those with ESRD who are managed conservatively. There is very limited evidence on the incidence or prevalence of conservative care of ESRD, and population-based needs assessments in relation to conservative care are rare. In 2011, a detailed whole population-based study was published in Australia to estimate the total incidence of ESRD (4), including (for the first time) both those treated with RRT and those receiving conservative care. Previous evidence on ESRD from the national and international renal registries has been limited to those with dialysis or transplant. The authors identified 21,500 new patients with ESRD in Australia during the period from 2003 to 2007 (4); this amounted to 21 patients per 100,000 people (20.9 per 100,000 population, with 95% confidence interval, 18.3 to 24.0 per 100,000 population). For

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Table 1. Definition of comprehensive conservative care

Comprehensive conservative care is planned (holistic patient-centered care for patients with stage 5 [GFR category 5] CKD) that includes:

Interventions to delay progression of kidney disease and minimize risk of adverse events or complications
 Shared decision making
 Active symptom management
 Detailed communication, including advance care planning
 Psychologic support
 Social and family support
 Cultural and spiritual domains of care
 Comprehensive conservative care does not include dialysis

Modified from Davison *et al.* (3), with permission.

every new patient who received dialysis or transplant, there was about one new patient who did not.

A community-based cohort study in Canada showed that, during median follow-up of 4.4 years of 1,816,824 adults with measured eGFR in Alberta, Canada, 5.36% died, with 0.18% who developed kidney failure treated and 0.17% who developed kidney failure managed conservatively (5). As in the Australian population-based study (4), for every new patient who received dialysis or transplant, there was about one new patient who did not, and rates of untreated kidney failure were consistently higher at older ages. Both studies indicate that the incidence of advanced kidney disease in older people may be higher than previously thought, and certainly, there are greater than expected rates of untreated kidney failure among the oldest patients. It may be that additional population-based studies in other countries would show similarly higher than expected levels of conservative management of ESRD.

In interpreting these findings, there are some major limitations. First, national data are only as yet available from Australia and Canada and may not apply to other countries and contexts. Second, just as dialysis patterns have changed over time, it is probable that patterns of conservative care have changed over time. It is worth noting that, in the Australian whole population-based study, neither the overall proportion of new patients managed with conservative care nor the age-standardized rate of conservative care consistently changed over the time period from 2003 to 2007, but this is a relatively short timeframe, and additional study across more extended time periods is needed. Third and perhaps most important of all, these data relate only to high-income countries; the limited availability of dialysis in some low- and middle-income countries may have a profound effect on the

apparent prevalence of conservative management and underlines the importance of defining and understanding the different sectors of the population that are managed without dialysis (as defined in Table 2).

What Is the Evidence on Survival in Conservative Care?

Another consideration is survival of those managed without dialysis. One of the main challenges in studying and comparing survival between dialysis and conservative populations is the bias inherent in the pathway decision. Those who are more fit usually opt for dialysis, and many choose or are advised to have conservative management because of comorbidity or other factors, which in themselves adversely influence survival. Without randomization into either group, it is difficult to attribute survival differences to either dialysis or conservative management.

Recent changes in dialysis practice, with lowering of the average eGFR for starting dialysis after the Initiation of Dialysis Early and Late Trial (6), mean that lower starting eGFRs to base comparative estimates of survival and quality of life between dialysis and nondialysis treatment pathways may be more feasible (7). We also need improved understanding of renal progression risk (particularly in older patients with low eGFR without proteinuria) to determine those least likely to benefit from dialysis.

In addition, many studies do not compare survival, hospital days and symptoms, or quality of life between the two populations; any meaningful comparison needs to consider not only survival, but also the nature of any additional days of survival. Days spent going to or staying in the hospital or with poor quality of life are not rated as highly by patients as hospital-free days and days with good quality of life (8,9).

Table 2. Distinct conservative care populations

- (1) Comprehensive conservative care: conservative care that is chosen or medically advised
- (2) Choice-restricted conservative care: conservative care for patients in whom resource constraints prevent or limit access to RRT; therefore, a choice for conservative care cannot be recognized
- (3) Unrecognized stage 5 (GFR category 5) CKD: CKD is present but has not been recognized or diagnosed; therefore, a choice for conservative care cannot be recognized

Modified from Davison *et al.* (3), with permission.

The key evidence on survival of patients managed conservatively can be distilled from 14 studies (10–23). These are excellently summarized in the systematic review by O'Connor and Kumar (24), with later studies by Da Silva-Gane *et al.* (20) and Hussain *et al.* (23). In the absence of randomized, controlled trials (ethically and practically difficult if not impossible), each of these studies is flawed in one way or another. Only about one half (11,12,15,16,18–20,23) compare survival between patients on conservative care and those on dialysis. The main flaws relate to significant differences in the comparison groups with regard to age profiles, how conservative/dialysis decisions were made, varying time from which survival is measured (including computing or assuming actual or putative dialysis start dates), likely changes in referral and dialysis practices over recent decades, and the reality that it is only truly legitimate to compare survival outcomes when each group is eligible for both treatment options (25). Some studies provide additional context for ESRD and report comorbidity or level of dependence/performance; however, scoring systems vary, and the Charlson score, in particular, may double count or overscore age. In contrast, frailty—which is very common in this population and independently associated with increased mortality—is rarely measured or reported (26).

An additional challenge is that the conservative care population is heterogeneous. It includes at least three groups of patients whose survival is likely to be very different: first, those suitable for dialysis who choose not to receive it; second, older people with high comorbidity who are not offered dialysis, and third, patients who lack capacity and may not always be offered dialysis. Although some of the studies try to make these distinctions, the numbers in the conservative management arms are often small and difficult to analyze with precision. In France, a multicenter, prospective cohort study of 581 older patients (mean age of 82 years old) with ESRD has shown that, despite a high prevalence of comorbidities, most patients are autonomous and living at home. At inclusion, 43% postponed the dialysis decision because of stable eGFR, 17% were under evaluation, 24% chose dialysis, and 16% decided not to have dialysis (27). Szeto *et al.* (22) present data on 25 patients who were considered suitable for but declined dialysis and contrasted this group with 38 patients who were not considered suitable for dialysis, mainly because of multiple coexisting medical illnesses. The former declining group was younger and less comorbid than the latter group, and yet, it had no difference in survival (22). Another confounder is that most studies do not address survival advantage/excess mortality of patients in relation to life expectancy of age-matched, period-specific individuals in the general population.

Among the key survival studies, the work by Joly *et al.* (11) studying those ≥ 80 years old is notable for long follow-up (up to 12 years), so that differences in referral patterns could be sought over different time periods. Those not put forward for dialysis were of similar age but more likely to be socially isolated, be referred later, be diabetic, and have poorer performance. Survival was significantly longer in the dialyzed group (28.9 versus 8.9 months). Usefully, the 2.4-year life expectancy of the dialyzed octogenarians was related to population norms and represented about one quarter to one third of the life expectancy of the general population >80 years old as

reported in national life expectancy statistics in France at the time. In contrast, the most widely cited paper by Smith *et al.* (12) is on the basis of very small numbers (10 and 26) comparing those recommended not to dialyze who nevertheless decided to dialyze with those who followed the recommended conservative pathway, respectively. Their finding of no significant survival advantage (8.3 versus 6.3 months) between these frail elderly patients was important, despite the small numbers and despite the fact that a putative dialysis initiation date was on the basis of eGFR of <10 ml/min estimated using the Cockcroft–Gault formula (12). In this study, 65% of the deaths occurring in the patients on dialysis took place in the hospital compared with 27% in the conservative group (used as a surrogate quality indicator).

Carson *et al.* (18) attempted to start the clock at an equivalent time in the comparative groups (all incident patients 70 years old and older) by computing putative dialysis start times (eGFR=10.8 ml/min per m^2), which mirrored practice in the dialysis group. They showed significant survival advantage in the dialyzed group (37.8 versus 13.9 months), but the conservative group was approximately 10 years older; statistical corrections could not be made to correct for this age difference because of the small numbers (18). The patients on conservative care were more likely to die at home or in a hospice (again, used as an indirect quality marker), and the authors computed that every day of additional survival was almost at the expense of a day spent either as an inpatient or attending the hospital for dialysis (hospitalization: 0.069 versus 0.043 hospital days per patient days survived) (18). A different approach was adopted by Murtagh *et al.* (15), who measured survival from eGFR <15 ml/min. They confined their analysis to all of those with stage 5 CKD >75 years old known to the nephrology clinic (15). Once again, the overall survival was better in the dialysis group, but this advantage was lost in patients with high comorbidity. There are a number of caveats to this study. No late presenters were included (and therefore, this may not reflect real life practice and cannot be compared with studies where all incident patients are included). The age of the conservative group was 4 years older than that of the dialysis group, and perhaps most importantly, the analysis was on an intention to treat basis; 24 patients (24 of 52) who chose the dialysis pathway did not actually receive dialysis by the study end either because they died ($n=8$) or because dialysis had not yet started ($n=16$).

Szeto *et al.* (22) reported on survival of 63 patients on conservative care, and although these authors did not attempt to compare conservative and dialysis groups, they do (like the work by Carson *et al.* [18]) provide useful data on the subgroup of patients who declined dialysis ($n=25$). These were, on average, a decade younger and had much lower comorbidity scores, but—importantly—their survival was not significantly different from the conservative group. The median survival from the date of needing dialysis (7 ml/min) was 6.58 months. Of note, only 36 of 63 were deemed to have died from uremia, with other unrelated deaths occurring both before ($n=12$) and after ($n=7$) the theoretical date of needing dialysis. Taking this study and inferring from other studies (11,12,18), there is fair evidence that the median survival from eGFR=6–7 ml/min is around 6 months.

The more recent papers (19,23) offer the best available evidence on survival. Work by Chandna *et al.* (19) spans an 18-year period and involved 844 patients, with 155 (18%) receiving conservative care. Patients on conservative care were older and had higher comorbidity. Again, there was an overall survival advantage to dialysis (mean survival of 21.2 versus 67.1 months; $P < 0.001$). However (as earlier studies had indicated but less robustly), for patients >75 years old, the survival advantage of dialysis reduced to only 4 months (nonsignificant) when corrected for age, high comorbidity, and diabetes. Similarly, in a retrospective observational study of comparative survival in patients over the age of 70 years old attending predialysis clinic, Hussain *et al.* (23) reported hospital admission and palliative care access outcomes between patients managed conservatively or choosing RRT. Survival, measured from three time points for both groups (eGFR <20 , <15 , and <12 ml/min), showed that dialysis conferred a significant survival advantage. However, there was a significant reduction in the effect of dialysis pathway on survival for those with high Charlson comorbidity index. Hospital admissions were greater and chances of dying at home were reduced in the patients on dialysis. There was no survival advantage from dialysis in >80 year olds with high comorbidity or poor functional status at all levels of disease severity.

What Are Symptoms, Quality of Life, and Illness Experiences in Conservative Care?

It is not only survival that is important but crucially, the symptoms, quality of life, and experience of illness on the conservative management pathway (8). Once again, there is limited evidence. The systematic review by O'Connor and Kumar (24) provides the best summary of evidence about symptoms and quality of life. Six studies describe symptom burden and/or quality of life. Most are cross-sectional in design, and all received a level 2—or intermediate—strength of recommendation taxonomy rating in the review (24,28). Three studies used the Memorial Symptom Assessment Schedule to collect data (29–31), whereas one study used the modified Palliative (or patient) Outcome Scale - Symptom module (32). Three articles directly measured quality of life (16,31,33) using standardized tools (either the Short Form 36 Health Survey Questionnaire or the EuroQoL EQ5D survey). One study also used interviews (16).

All report significant symptom burden in those undergoing conservative care, with numbers of symptoms varying from 6.8 to 17 per individual patient. These studies were remarkably consistent in terms of reporting similar symptoms and similar patterns of prevalence. Where reported, there was a considerable increase in symptoms in the month before death (30). Evidence on management of symptoms is the accompanying articles by Davison and Jassal in this Moving Points feature (34). Three of the studies (16,31,33) included a comparison group. Since the systematic review of this evidence, Da Silva-Gane *et al.* (20) have published additional evidence reporting quality of life assessments every 3 months for up to 3 years in patients with advanced progressive CKD (late stage 4 or early stage 5) managed conservatively or by dialysis. This is the only longitudinal study that contrasts conservative and

dialysis management; patients on conservative care were older, more dependent, and more highly comorbid with poorer physical health and higher anxiety levels than patients on dialysis. Their most important finding, however, was that the patients on conservative care maintained quality of life, whereas life satisfaction decreased significantly after dialysis initiation in the dialysis group. Mental health, depression, and life satisfaction scores were overall similar in the two groups at the start of the study. Brown *et al.* (7) have also reported survival, symptom burden, and quality of life in conservatively managed patients, including 273 patients predialysis who had usual nephrology care and 122 patients on the nondialysis pathway who also attended a renal supportive care clinic. Median survival in the latter group was 16 (interquartile range, 9–37) months. With the renal supportive care clinic input, 57% of the patients not on dialysis had stable or improved symptoms over 12 months, and 58% had stable or improved quality of life.

Although O'Connor and Kumar (24) have proposed that additional head to head studies are needed to compare the symptoms of age-matched patients on dialysis, they also felt that the current available studies suggested that quality of life was not significantly different in patients on conservative care and patients on dialysis. The more recent work by Da Silva-Gane *et al.* (20) confirms this, and the work by Brown *et al.* (7) suggests that renal supportive care clinics can be effective in controlling symptoms and maintaining quality of life, although the specific interventions need additional study.

Beyond physical and psychologic symptoms and quality of life, spiritual care needs have also been considered, although critically, in all patients with advanced kidney disease rather than specifically in the conservative population. In a prospective cohort study of 253 patients with stage 4 or 5 CKD or on dialysis in Canada, patients reported a mean of 2.9 ± 2.6 spiritual needs, with 69% of patients reporting at least one spiritual need; 32% of patients had high spiritual needs (defined as reporting five or more of the seven needs). Spiritual needs were associated with age, sex, race, marital status, dialysis modality, time on dialysis, or comorbidity (35). Another study using the same cohort found that adjustment in the domains of psychologic distress and extended family relationships seems to mediate some of the beneficial effect of existential well-being on health-related quality of life. Spirituality, however, provides unique variance in patients' quality of life independent of their psychosocial adjustment (36).

A final piece of important evidence relates to the effect on family of caring for someone with CKD stage 5. Work undertaken in the United Kingdom (37) investigated this and identified confusion about the nature of conservative kidney management. Caregivers were not aware of the palliative nature of conservative care or the approaching end of life issues, and this highlighted some of their unmet support needs. This resonates with evidence directly from patients themselves: that patients' expectations of conservative care are strongly influenced by what is communicated to them by renal staff (38). Even in renal units with established conservative care pathways, there is often only limited information available to patients and families about illness progression and what to expect as the illness progresses.

Conclusions

Evidence on conservative care remains limited. The best evidence is on survival. This does not necessarily reflect what matters most to patients with ESRD and their families; instead, it reflects what has been studied to date. The published comparative survival outcomes between dialysis and conservative management suffer from inherent methodologic flaws that limit any conclusions.

There is no doubt that—in general—dialysis is associated with a significant survival advantage, but this advantage reduces notably for older people with major comorbidity and poorer functional status, with little or no survival benefit for older people (>75 years old), people with high comorbidity scores, and people with poor functional status. Quality of life, symptoms, and hospital-free survival may be at least as important to consider and actively manage. Before starting kidney replacement therapy, there should be a shared decision-making process on the basis of understanding of the prognosis, the potential benefits and harms of therapy, and the patient values, goals, and preferences (39). The best models of care or interventions for those managed conservatively without dialysis are not yet known. The limited evidence on cost-effectiveness is summarized in the accompanying article by Morton and colleagues in this Moving Points feature (40) but additional study of the best ways to improve and maintain quality of life as well as survival is needed.

The perspectives on comprehensive conservative care may vary between countries according to the availability of RRT—this is important, and characterizing the different conservative care populations can help. However, there is consensus on how comprehensive conservative care can be defined and what it includes, and adopting this definition and consistency in what is delivered will help to support service development and future research. The use of a standard definition will provide both clinicians and researchers a framework for moving the field forward.

Research now needs to incorporate changes in dialysis practice, with comparative studies of survival and quality of life allowing for the lower average eGFR of dialysis start. We need improved evidence about renal progression risk to further determine those least likely to benefit from dialysis. Although there is clear evidence of symptom burden and poor quality of life with conservative management, the interventions and models of care that best address these issues have yet to be determined; this research must be addressed from patient and family perspectives if it is to deliver greatest effect.

Disclosures

None.

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