



Risk Factors for Unplanned Dialysis Initiation: A Systematic Review of the Literature

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Abstract

Background: Unplanned dialysis initiation is common in patients with chronic kidney disease (CKD).

Objective: To determine common definitions and patient risk factors for unplanned dialysis.

Design: Systematic review.

Setting: MEDLINE, EMBASE, and the Cochrane Library were searched from inception to February 2018.

Patients: Studies that included incident chronic dialysis patients or patients with CKD that cited a definition or examined risk factors for unplanned dialysis were included.

Measurements: Definitions and criteria for unplanned dialysis reported across studies. Patient characteristics associated with unplanned dialysis.

Methods: Two reviewers independently extracted data using a standardized data abstraction form and assessed study quality using a modified New Castle Ottawa Scale.

Results: From 2797 citations, 48 met eligibility criteria. Reported definitions for unplanned dialysis were variable. Most publications cited dialysis initiation under emergency conditions and/or with a central venous catheter. The association of patient characteristics with unplanned dialysis was reported in 26 studies, 18 were retrospective and 21 included incident dialysis patients. The most common risk factors in univariate analyses were (number of studies) increased age (n = 7), cause of kidney disease (n = 6), presence of cardiovascular disease (n = 7), lower serum hemoglobin (n = 9), lower serum albumin (n = 10), higher serum phosphate (n = 6), higher serum creatinine or lower estimated glomerular filtration rate (eGFR) at dialysis initiation (n = 7), late referral (n = 5), lack of dialysis education (n = 6), and lack of follow-up in a predialysis clinic prior to dialysis initiation (n = 5). A minority of studies performed multivariable analyses (n = 10); the most common risk factors were increased age (n = 4), increased comorbidity score (n = 3), late referral (n = 5), and lower eGFR at dialysis initiation (n = 3).

Limitations: Comparison of results across studies was limited by inconsistent definitions for unplanned dialysis. High-quality data on patient risk factors for unplanned dialysis are lacking.

Conclusions: Well-designed prospective studies to determine modifiable risk factors are needed. The lack of a consensus definition for unplanned dialysis makes research and quality improvement initiatives in this area more challenging.

Abrégé

Contexte: L'initiation non planifiée d'un traitement de dialyse est fréquente chez les patients atteints d'insuffisance rénale chronique (IRC).

Objectifs: L'étude visait à définir la dialyse non planifiée et à définir ses facteurs de risques chez les patients.

Type d'étude: Une revue systématique.

Sources: Les bases de données MEDLINE et EMBASE, de même que la bibliothèque Cochrane ont été consultées, de leur création à février 2018.

Sujets: Les études traitant de patients atteints d'IRC ou dialysés de façon chronique, et qui citaient une définition ou examinaient les facteurs de risques associés à une dialyse non planifiée.

Mesures: On a colligé les différentes définitions d'une dialyse non planifiée rapportées dans l'ensemble des études, ainsi que les critères la définissant et les caractéristiques des patients qui y étaient associées.

Méthodologie: À l'aide d'un formulaire normalisé d'extraction des données, deux examinateurs ont compilé les données de façon indépendante. La qualité des études a été évaluée avec une échelle de Newcastle-Ottawa modifiée.



Résultats: Des 2 797 études répertoriées, 48 satisfaisaient les critères d'admissibilité. Les définitions d'une dialyse non planifiée variaient d'une étude à l'autre. La plupart des publications mentionnaient une dialyse débutée en situation d'urgence et/ou avec un cathéter veineux central. L'association des caractéristiques des patients à une dialyse non planifiée a été signalée dans 26 études, desquelles 18 constituaient des études rétrospectives et 21 incluaient des patients dialysés incidents. Les facteurs de risque les plus souvent cités dans les analyses univariées étaient (en nombre d'études) : l'âge avancé du patient (n=7), la cause de la néphropathie (n=6), la présence d'une cardiopathie (n=7), de faibles taux d'hémoglobine (n=9) et d'albumine (n=10), un taux élevé de phosphate sérique (n=6), un taux élevé de créatinine sérique ou un faible DFGe à l'amorce de la dialyse (n=7), un aiguillage tardif (n=5), le manque d'information sur la dialyse (n=6), et l'absence de suivi dans une clinique de pré-dialyse avant l'initiation du traitement (n=5). Seules quelques études avaient procédé à des analyses multivariées (n=10). Dans ces dernières, les facteurs de risques les plus fréquemment cités étaient : l'âge avancé du patient (n=4), un score de comorbidité élevé (n=3), un aiguillage tardif (n=5), et un faible DFGe au moment de l'initiation de la dialyse (n=3).

Limites: La comparaison des résultats d'une étude à l'autre était difficile en raison d'un manque d'uniformité dans les définitions d'une dialyse non planifiée. On manque de données robustes sur les facteurs de risque menant à une dialyse non planifiée chez les patients.

Conclusion: On constate un besoin pour des études prospectives bien conçues examinant les facteurs de risque modifiables. L'absence d'une définition consensuelle pour la dialyse non planifiée rend plus difficiles les initiatives de recherche et d'amélioration de la qualité dans ce domaine.

Keywords

systematic review, dialysis, risk, predialysis, CKD

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What was known before

Unplanned dialysis initiation is common in patients with chronic kidney disease. Determining patient risk factors for this important outcome may help reduce the incidence.

What this adds

High-quality data on patient risk factors for unplanned dialysis are lacking. Well-designed prospective studies to determine modifiable risk factors are needed.

Introduction

Many patients with chronic kidney disease (CKD) start dialysis in an unplanned fashion and/or under urgent circumstances despite regular follow-up by a nephrologist. Most studies report a prevalence of unplanned dialysis between 40% and 60%.¹⁻⁷ However, the prevalence varies, likely in large part due to inconsistent definitions across studies. An unplanned dialysis start is defined by varying criteria that may include dialysis initiation with a central venous catheter (CVC) as opposed to a permanent access (arteriovenous fistula, arteriovenous graft, or peritoneal dialysis catheter), and/or dialysis initiation during an acute hospitalization, and/or dialysis

initiation under emergent circumstances.⁷ Unfortunately, there is no established consensus definition.

Unplanned dialysis is of concern because, theoretically, patients forego the opportunity to make an informed, shared decision with respect to timing and modality of renal replacement therapy (RRT). Instead, most centers in North America only offer one option for RRT under urgent conditions: hemodialysis with a CVC. In addition, unplanned dialysis is associated with increased patient morbidity and mortality and added health care costs.^{4,6-9} Given the high prevalence of unplanned dialysis and association with poor patient outcomes, we conducted a systematic review to determine patient risk factors for this outcome. As a secondary objective, we determined the most common criteria and terminology used to define the outcome. The results of this systematic review should help to inform future studies aimed at reducing the burden of unplanned dialysis starts.

Materials and Methods

Search Strategy

We performed a comprehensive, systematic search of articles published in peer-reviewed journals using MEDLINE, EMBASE, and the Cochrane Library (from inception to

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February 28, 2018). The search was carried out with the assistance of a librarian experienced in systematic reviews. We used a structured search strategy (outlined in Supplementary Appendix A), based on controlled vocabulary and relevant key terms that were broad to prioritize sensitivity. The references of included articles and existing reviews were scanned for additional studies. There were no restrictions based on study design or language in the search.

Study Selection

There were 2 independent investigators (A.O.M. and A.A.) who screened identified titles and abstracts. Those deemed to be clearly irrelevant were removed on the initial screen. If no abstract was available, the full text was obtained unless the article could be confidently excluded by title alone. Full-text versions of potentially eligible studies were obtained and independently screened by 2 reviewers (A.O.M. and R.H. or A.A.) to determine their eligibility based on the selection criteria. Any disagreements during the screening process were resolved through discussion among the authors in accordance with the selection criteria.

We included retrospective and prospective studies that reported criteria to define unplanned dialysis or characteristics of patients who had an unplanned versus planned dialysis start. We excluded non-English articles, studies published only in abstract form, case reports, narrative reviews, editorials, letters, practice guidelines, and pediatric studies. We excluded studies that focused primarily on late referral to nephrology.

Data Extraction and Synthesis

Two independent investigators (A.O.M. and R.H.) abstracted data using a standardized data abstraction form (see Supplementary Appendix B). The following data were abstracted: study methods, patient characteristics, criteria and terminology used to define unplanned dialysis, and patient characteristics by unplanned versus planned dialysis status. Patient characteristics significantly associated with unplanned dialysis were summarized, along with covariates included in multivariable models to identify independent associations. Statistical significance within studies was defined by individual study methods. Two investigators (A.O.M. and R.H.) independently performed a quality assessment for studies that reported patient characteristics associated with unplanned dialysis. A modified Newcastle-Ottawa Scale (NOS) was used to assess the quality of applicable observational studies.¹⁰ A score was given for the NOS domains of cohort selection and comparability (maximum scores of 4 and 2, respectively). The outcome domain was removed from the NOS, as we did not examine outcomes associated with unplanned dialysis. The reporting of this systematic review is in accordance with PRISMA guidelines (refer to Supplementary Appendix C for details).¹¹ The

methods were all prespecified, and the review protocol was registered with the international prospective register of systematic reviews (<http://www.crd.york.ac.uk/PROSPERO>; registration no. CRD42016032916).¹²

Results

Eligible Studies

Study selection is outlined in Figure 1. The electronic database search identified 2843 records and one further record was identified from other sources. There were 2798 nonduplicate citations. After independently reviewing the title and abstract of all potentially relevant records, 407 articles were retrieved and reviewed in full text. Of these articles, 48 studies were found to meet inclusion criteria.

Patient and Study Characteristics

The characteristics of the 48 eligible studies are outlined in Table 1. Eligible studies included incident chronic dialysis patients (n = 42)^{2-4,6,8,9,13-48} and patients with CKD known to nephrology (n = 6).^{5,49-53} Study designs included retrospective cohort studies (n = 27),^{2,3,5,6,14-16,19-24,26,28,31-36,38,47-50,53} cross-sectional studies (n = 2),^{9,52} prospective cohort studies (n = 17),^{4,8,17,18,25,27,29,30,37,39-45,51} retrospective before/after studies (n = 1),⁴⁶ and unclear design (n = 1).¹³ No randomized control trials were found in the search. The majority of studies were conducted in Europe (n = 26; 22 unique cohorts)^{2,8,9,15-19,22-25,29,30,33,36,40-43,45-48,50,51}; 11 studies were conducted in North America^{3-6,14,21,26,28,31,52,53} (Canada, n = 9; 8 unique cohorts). Study cohort sizes ranged from 43 to 45 785 persons.

Terms and Definitions for Unplanned Dialysis

The terminology used to describe an unplanned dialysis start was variable across studies (Table 1). Examples of terminology included unplanned dialysis, urgent dialysis, unscheduled dialysis, and suboptimal dialysis start. Varying criteria were used to define unplanned dialysis; however, all definitions included some consideration of the conditions under which dialysis was started (ie, during a hospitalization or emergently) and/or the access that was used at dialysis initiation (ie, a CVC) (Table 1, Figure 2). The proportion of patients with an unplanned dialysis start differed across studies, ranging from 7% to 100%, but most studies reported a proportion between 40% and 60% (n = 21).^{2,3,5,6,14,15,19,23,24,26-31,36,38,48,51-53}

Patient Risk Factors for Unplanned Dialysis

There were 26 studies (25 unique cohorts) that reported the association of patient characteristics with unplanned dialysis, 21 of which included incident chronic dialysis patients (retrospective cohort study, n = 15; cross-sectional study, n

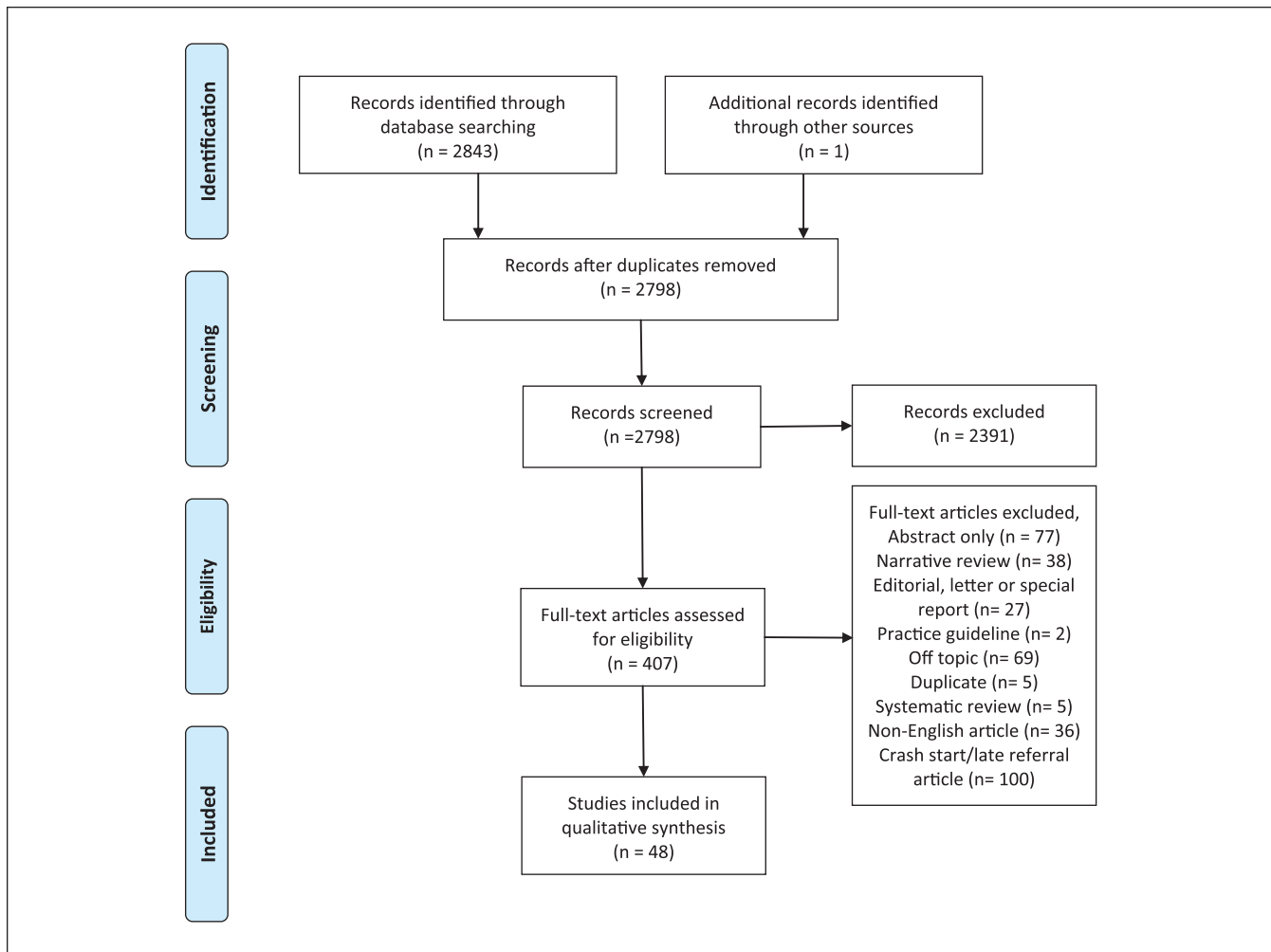


Figure 1. Study selection.

= 1; prospective cohort study, n = 5),^{2-4,6,8,9,15,19,21-28,31,34,38,39,48} and 5 of which included patients with CKD known to nephrology (retrospective cohort study, n = 3; cross-sectional study, n = 1; prospective cohort study, n = 1)^{5,49,51-53} (Table 1). Determining patient risk factors for unplanned dialysis was listed as an objective in 12 studies; all of these studies were retrospective or included incident dialysis patients.^{2-5,19,21,23,24,26,39,48,53}

There were 24 studies that reported patient characteristics by unplanned versus planned dialysis status using descriptive, univariate analysis.^{2-6,8,9,15,19,21-28,34,38,39,48,51-53} Supplementary Table 1 summarizes the characteristics reported across studies and whether the characteristic significantly differed, based on a P value $< .05$, between patients with an unplanned versus planned dialysis start. All characteristics significantly associated with unplanned dialysis ($P < .05$) in univariate analysis are summarized in Table 2. The most common risk factors in univariate analysis were (number of studies) increased age (n = 7),^{3,5,6,24,25,28,38} cause of kidney disease (n = 6),^{3,5,23,24,48,53} congestive heart failure (n = 5),^{3,5,9,39,53} cardiovascular

disease (n = 7),^{3-6,9,28,53} lower serum hemoglobin (n = 9),^{2,3,6,9,15,23,24,27,39} lower serum albumin (n = 10),^{2,3,6,15,23-25,39,48,53} lower serum calcium (n = 5),^{6,15,23,24,48} higher serum phosphate (n = 6),^{2,6,15,24,39,48} higher serum creatinine or lower eGFR/creatinine clearance at dialysis initiation (n = 7),^{2,6,15,23-25,48} late referral to a nephrologist (n = 6),^{3-5,27,28,52} lack of dialysis education (n = 6),^{2,23,24,39,48,53} and not followed in a dedicated predialysis clinic prior to dialysis initiation (n = 5).^{2,15,24,26,38} There was one study that reported a higher eGFR and lower serum creatinine in patients with an unplanned dialysis start.⁵³ For cause of kidney disease, polycystic kidney disease, all genetic kidney disease, and glomerulonephritis were less common in patients with an unplanned start.^{3,15,24,53} Nephrosclerosis, renal artery stenosis, and diabetic nephropathy were more common in patients with an unplanned start.^{3,5,53}

There were 10 studies that used multivariable analysis or propensity matching to examine the association of patient characteristics with unplanned dialysis.^{2-5,26,31,39,48,49,53} All patient characteristics significantly associated with unplanned

Table 1. Study Characteristics.

Study	Study design	Participants/number of centers/country	Exclusion criteria	Number of participants with an unplanned dialysis start, n (%)	Mean (SD) age of participants	Definition of unplanned dialysis/terminology used	Patient characteristics reported by unplanned versus planned dialysis (y/n)	Adjusted analysis of characteristics associated with unplanned dialysis (y/n)
Holland and Lam ⁵	RCS	201 patients age > 16 years with progressive CKD followed in a predialysis clinic who began dialysis during the study period//Canada	None specified	91 (45)	62	Dialysis initiation during a hospitalization/suboptimal dialysis start	Yes	Yes
Mercalfe et al. ²⁵	PCS	532 incident chronic dialysis patients//United Kingdom	Preemptive kidney transplant	129 (24)	65 (16-91) ^a	Followed by nephrology for ≥ 1 month, steady progression to ESRD and no permanent access at dialysis initiation/unplanned dialysis start	Yes	No
Abderahim et al. ¹³	Unclear	299 patients with diabetes initiating chronic dialysis//Tunisia	Reversible AKI, nondiabetic nephropathy	104 (35)	58 (9) ^b 35 (7) ^c	Dialysis started in emergency conditions (unspecified)/urgent or emergency onset of RRT	No	No
Caskey et al. ⁸	PCS	196 incident chronic dialysis patients known to nephrology for at least 1 month before starting RRT//7 European countries	None specified	70 (36)	62 (46-71) ^d	No previous creatinine > 300 μmol/L or first dialysis not arranged in advance and performed urgently for life-threatening renal insufficiency/unplanned dialysis	Yes	No
Joly et al. ²⁰	RCS	144 incident octogenarians with CKD and calculated CrCl < 10 mL/min referred to a renal unit//France	Death prior to therapeutic decision	35 (24)	83 (3)	Emergency dialysis (no further details)/unplanned dialysis	No	No
Loos et al. ⁹	Cross-sectional	169 hospitalized incident chronic dialysis patients ≥ 70 years with a predialysis CrCl < 15 mL/min or creatinine > 600 μmol/L//France	None specified	78 (66)	76 (5)	No specific criteria provided/unplanned dialysis	Yes	No
Ravani et al. ^{29,30}	PCS	229 incident chronic dialysis patients//Italy	None specified	103 (45)	64 (15)	Development of uremic complications that required an emergency dialysis start/unplanned dialysis	No	No
Frimat et al. ¹⁸	PCS	148 incident chronic dialysis patients with diabetes//13/France	Acute, reversible renal failure, kidney graft failure	87 (59)	79 (44-89) ^e	Dialysis not initiated with an arteriovenous fistula/graft or a Tenckhoff catheter/unplanned dialysis	No	No
Marron et al. ²³	RCS	621 incident chronic dialysis patients//Spain	None specified	304 (49)	62 (15)	Uremia requiring emergency initiation of dialysis/nonplanned dialysis start	Yes	No
Castellano et al. ¹⁵	RCS	117 incident chronic dialysis patients//Spain	None specified	52 (44)	64 (15)	Dialysis started for an emergency condition or it was not appropriate to delay starting dialysis for > 24 hr/nonprogrammed dialysis	Yes	No
Marron et al. ²⁴	RCS	1504 incident chronic dialysis patients//35/Spain	None specified	695 (46)	61 (16)	Dialysis start unscheduled, even if a permanent access was in place/nonplanned dialysis start	Yes	No
Buck et al. ²	RCS	109 patients initiating RRT known to renal services for at least 4 months//1 tertiary center and 4 satellite dialysis units//United Kingdom	No consent for data collection	49 (45)	63	Dialysis started using a catheter or during an emergent hospitalization/known acute dialysis	Yes	Yes
Couchoud et al. ¹⁶	RCS	3512 incident chronic dialysis patients ≥ 75 years//multiple centers//France	AKI	1134 (32)	80 (75-100) ^g	First HD started under emergency conditions (dialysis required within 24 hr)/unplanned HD	No	No
Thilly et al. ²³	RCS	1315 incident chronic dialysis patients//13/France	AKI	559 (43)	67 (15)	HD with a temporary catheter/unplanned dialysis	No	No
Wu et al. ¹⁴	RCS	486 incident chronic HD patients surviving > 90 days following dialysis initiation//Taiwan	None specified	368 (76)	Not available	Vascular access creation after HD initiation/urgent dialysis	Yes	No
Yoon et al. ³⁵	RCS	503 incident HD patients//8/South Korea	None specified	412 (82)	59 (16-93) ^g	Initiation of HD without prior placement of a permanent access/unplanned dialysis	No	No
Crews et al. ⁴	PCS	652 incident chronic dialysis patients able to speak English or Spanish//7/USA	Incomplete data on location of dialysis	410 (63)	59 (14) ^h 60 (15) ^h	HD initiation during a hospitalization/impatient HD start	Yes	Yes (1 characteristic)
Teo et al. ³²	RCS	168 incident chronic dialysis patients surviving more than 90 days on dialysis//Singapore	None specified	109 (65)	59 (14)	Immediate HD using a catheter/urgent dialysis	No	No
Gomis Couto et al. ¹⁹	RCS	43 incident HD patients//Spain	PD, kidney graft failure	20 (47)	61 (32-85) ^g	Dialysis initiated with a temporary venous catheter/unscheduled dialysis	Yes	No
Descamps et al. ¹⁷	PCS	495 incident chronic dialysis patients//France	AKI	167 (34)	62 (16)	Unplanned first dialysis session/emergency dialysis	No	No

(continued)

Table 1. (continued)

Study	Study design	Participants/number of centers/country	Exclusion criteria	Number of participants with unplanned dialysis start, n (%)	Mean (SD) age of participants	Definition of unplanned dialysis/terminology used	Patient characteristics reported by unplanned dialysis (y/h)	Adjusted analysis of characteristics associated with unplanned dialysis (y/h)
Mendissohn et al ⁶	RCS	339 incident chronic dialysis patients or preemptive kidney transplants/10/Canada	Temporary RRT due to drug or environmental intoxication, AKI treated in the ICU, RRT initiation due to kidney transplant rejection	205 (61)	63 (16)	Dialysis started with a CVC or during a hospitalization/suboptimal dialysis start	Yes	No
Piwko ²⁸ (subcohort of Mendissohn et al ⁶)	RCS	323 incident chronic dialysis patients/10/Canada	Temporary RRT due to drug or environmental intoxication, AKI treated in the ICU, RRT initiation due to kidney transplant rejection	200 (62)	64 (15)	Dialysis started with a CVC or during a hospitalization/suboptimal dialysis start	Yes (1 characteristic)	No
Chiu et al ³	RCS	377 incident chronic dialysis patients/2/Canada	Requiring RRT for <3 months	221 (59)	66 (19-100) ^a	Dialysis started during a hospitalization or with a CVC following at least 1 outpatient consult with a nephrologist/suboptimal dialysis start	Yes	Yes
Cho et al ¹⁹	RCS	298 adults with an eGFR <40 followed for at least 3 months in the nephrology clinic//South Korea	Graft failure, AKI, prior RRT, recently diagnosed cancer	49 (16)	58 (14)	Unplanned initiation of dialysis due to uremia at the emergency room/urgent dialysis	No	Yes (1 characteristic)
Hdez-Odonez et al ²⁰	RCS	51 incident PD patients with an unplanned initiation requiring hospitalization//Mexico	Prior HD treatment	51 (100)	49 (19)	No peritoneal dialysis-related clinic visits in the 3 months prior to dialysis initiation/unplanned dialysis	No	No
Hughes et al ²¹	RCS	436 incident chronic dialysis patients 3/Canada	Missing data	304 (70)	67 (16)	Dialysis initiation during a hospitalization or with a CVC/suboptimal dialysis start	Yes	No
Lobbedez et al ²²	RCS	8499 incident PD patients/144/France	Primary PD failure, previously treated with PD, treated with HD for >30 days prior to PD, stopped PD because of renal recovery	568 (7)	71 (56-80) ^{df} 69 (50-79) ^{dg}	On HD for <30 days before peritoneal dialysis initiation (surrogate)/suboptimal dialysis start	Yes	No
Nadeau-Fredette et al ²⁶	RCS	95 patients with CKD who transitioned directly to home HD or were within 30 days of HD initiation//Canada	None specified	51 (54)	48 (14) ^f 44 (14) ^g	Initiation of dialysis with a CVC or during a hospitalization/suboptimal dialysis start	Yes	Yes
Singhal et al ¹	RCS	12 143 incident chronic dialysis patients/multicenter/Canada	No outpatient nephrology visit prior to RRT, recovered renal function, residing in a long-term care facility	5464 (45)	65 (52-74) ^h	Inpatient dialysis initiation	No	Yes
Al-Jaishi et al ¹⁴	RCS	17 183 adults initiating chronic HD/97/Canada	Missing data	7655 (45)	66 (15)	Dialysis as an inpatient within 2 weeks of starting RRT/acute dialysis	No	No
Arora et al ⁵²	Cross-sectional	249 patients with documented CKD (eGFR <60 on 2 occasions) who saw a nephrologist and started dialysis during the study period/multi-center/USA	Missing data	129 (52)	72 ⁱ	At least 2 predialysis eGFR values <60 mL/min/1.73 m ² , dialysis dependence after 90 days and initiated dialysis during a hospitalization/renal "crash" patient	Yes (1 characteristic)	No
Brown et al ⁵³	RCS	184 adults initiating chronic dialysis followed in a multidisciplinary CKD clinic prior to dialysis initiation//Canada	None specified	76 (41)	61 (16) ^j 65 (16) ^k	Dialysis initiation in hospital/unplanned dialysis	Yes	Yes
Park et al ²⁷	PCS	643 incident chronic dialysis patients ≥20 years/31/Korea	Missing data	295 (46)	55 (14)	Dialysis initiated with a CVC or without education about dialysis/unplanned dialysis	Yes	No
Prieto-Yelasco et al ⁵¹	PCS	1044 patients followed in CKD clinics/26/Spain	None specified	476 (46)	67 (56-77) ^l	Previously unknown by the nephrology unit and/or started dialysis in an urgent situation and/or without permanent access and/or without having gone through a dialysis educational program/unplanned dialysis	Yes (1 characteristic)	No
Jin et al ³⁷	PCS	178 patients with ESRD who required urgent initiation of dialysis without pre-established functional vascular access or a PD catheter//China	Unable to tolerate PD catheter insertion or wait time to undergo PD catheter insertion	178 (100)	53 (19)	Refer to inclusion criteria/urgent start dialysis	No	No

(continued)

Table 1. (continued)

Study	Study design	Participants/number of centers/country	Exclusion criteria	Number of participants with unplanned dialysis start, n (%)	Mean (SD) age of participants	Definition of unplanned dialysis/terminology used	Patient characteristics reported by unplanned versus planned dialysis (y/n)	Adjusted analysis of characteristics associated with unplanned dialysis (y/n)
Marron et al ⁴⁸	RCS	547 patients starting maintenance dialysis for CKD stage 5/25/Poland, Hungary, Romania	Preemptive kidney transplant	316 (58)	64 (42-81) ^d	Functional permanent access lacking or urgent start dialysis even if a permanent dialysis access was in place/nonplanned dialysis	Yes	Yes
Panocchia et al ⁴⁵	PCS	316 patients with CKD who were hospitalized, diagnosed with ESRD and started unplanned, urgent HD//Italy	AKI, prior history of RRT, multiple organ failure, coma, and dementia	316 (100)	67 (12)	Criteria not specified/unplanned, urgent HD	No	No
Kanno et al ³⁸	RCS	122 patients ≥85 years initiating HD//Japan	Recovery of renal function, received HD once then withdrew	69 (57)	87 (3)	HD initiation in an unplanned setting with a temporary noncuffed and nontunneled CVC, without preparation or use of a permanent access/suboptimal dialysis CVC/emergent start	Yes	No
Li et al ³⁹	PCS	507 incident ESRD patients //Taiwan	None specified	348 (69)	62 (16)	Acute dialysis for uremic emergency via a temporary CVC/emergent start	Yes	Yes
Machowska et al (4 studies, all the same patient population) ⁴⁶⁻⁴⁹	PCS	270 patients with CKD stage 5, aged between 18 and 90 years starting dialysis in an unplanned way//Austria, Germany, Denmark, France, United Kingdom, Sweden	AKI, conservative kidney care, acute conditions precluding participation, life expectancy <6 months	270 (100)	69 (40-83) ^d	Presented to nephrology within 1 month of needing dialysis and/or being followed by a nephrologist but requiring urgent dialysis by CVC or acutely placed PD catheter/unplanned dialysis	No	No
Magalhaes et al ⁴⁴	PCS	424 patients admitted to the emergency room with uremia and immediate need for dialysis (within 24 hr of presentation) //Brazil	Kidney transplant, taking vitamin D, prior RRT, recovered renal function	424 (100)	50 (18)	Refer to inclusion criteria/urgent start dialysis	No	No
Schanz et al ⁴⁶	Retrospective before/after study	336 adults initiating dialysis during the study time frame and with availability of data and knowledge of implemented dialysis modality//Germany	None specified	106 (70) preintervention and 113 (61) postintervention	69 (67-71) ^b preintervention 68 (66-70) ^b postintervention	Admitted to hospital with an acute deterioration of renal function reaching ESRD or with generally accepted acute indications for dialysis without a known prior history of ESRD/unplanned dialysis	No	No
Vigneau et al ⁴⁷	RCS	45 785 patients with ESRD undergoing dialysis/multicenter/France	AKI	13 736 (30)	71 ^a	Any first treatment occurring under life-threatening circumstances that requires dialysis initiation within 24 hr/emergency dialysis	No	No
Bechade et al ³⁶	RCS	74 adult patients with incident cancer who initiated dialysis following their cancer diagnosis/multi-center/France	Prior history of cancer, AKI, dialysis prior to cancer diagnosis, history of kidney transplant	34 (47)	68 (11)	Dialysis initiation using a temporary nontunneled CVC/unplanned dialysis	No	No

Note. RCS = retrospective cohort study; CKD = chronic kidney disease; PCS = prospective cohort study; ESRD = end-stage renal disease; AKI = acute kidney injury; RRT = renal replacement therapy; CrCl = creatinine clearance; HD = hemodialysis; ICU = intensive care unit; CVC = central venous catheter; eGFR = estimated glomerular filtration rate; PD = peritoneal dialysis.

^aMedian age (range).

^bPatients with type 2 diabetes.

^cPatients with type 1 diabetes.

^dMedian age (interquartile range).

^eMean age (range).

^fPlanned dialysis initiation.

^gUnplanned dialysis initiation.

^hMean age (95% confidence interval).

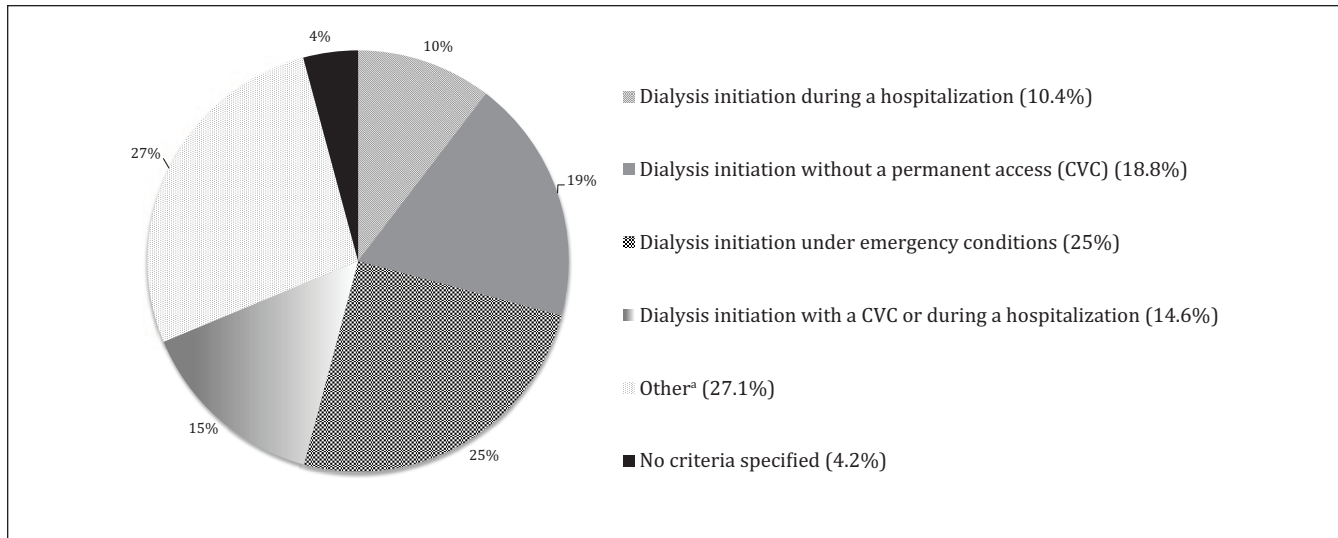


Figure 2. Definitions for unplanned dialysis among included studies (N = 48).

Note. CVC = central venous catheter; eGFR = estimated glomerular filtration rate.

^aMost of the criteria in the “other” category include criteria composed of a combination of all other categories ± preexisting eGFR criteria or referral to nephrology within a specified time period prior to dialysis initiation.

dialysis in multivariable or matched analyses ($P < .05$) are summarized in Table 3. The most commonly reported risk factors were increased age ($n = 4$),^{2,3,5,31} increased comorbidity score ($n = 3$),^{3,26,31} late referral to nephrology ($n = 5$),^{3,5,31,48} and lower eGFR at dialysis initiation ($n = 3$).^{2,39,48} Less cumulative nephrology care and less care during the period shortly prior to dialysis initiation (critical period) were significant in adjusted analyses ($n = 1$), as were other potential markers of quality of care (care in a predialysis clinic [$n = 1$] and dialysis education [$n = 1$]).^{2,31,49}

Hughes et al²¹ examined potential underlying causes for unplanned dialysis in patients referred to a nephrologist >12 months prior to dialysis initiation and found the following causes of unplanned dialysis: patient-related delays (31%), acute on chronic kidney injury (31%), surgical delays (16%), late decision-making by the nephrologist (8.6%), and other (12.5%). Marron et al⁴⁸ also examined reasons for unplanned dialysis and found a similar result, despite being conducted in another country: patient-related delays (36%), acute on chronic kidney injury or more rapid decline in eGFR than anticipated (28%), health care bureaucracy issues (11%).

Assessment of Study Quality

Study quality was assessed for the 26 studies that reported patient characteristics and their association with unplanned dialysis.^{2-6,8,9,15,19,21-28,31,34,38,39,48,49,51-53} One of the 26 studies was a secondary analysis of the Mendelssohn et al study.²⁸ Study quality reported using a modified NOS is summarized in Supplementary Table 2. Only one study was awarded all 4 possible points for cohort selection. Unfortunately, this study was not primarily designed to

examine risk factors for unplanned dialysis.⁵¹ Most studies lost a point for cohort selection because they were retrospective or included incident dialysis patients. The studies by Nadeau-Fredette et al,²⁶ Kanno et al,³⁸ and Loos et al⁹ lost 2 points for cohort selection because they only included home hemodialysis and very elderly patients, which are both a select group of patients. There were 16 studies that received 0 points for comparability because the study design or analysis did not address potential confounding, meaning that no form of statistical adjustment or matching was performed.^{6,8,9,15,19,21-25,27,28,34,38,51,52}

Discussion

This systematic review of literature published until February 2018 includes 48 studies that outlined criteria for unplanned dialysis, of which 26 studies reported patient characteristics associated with unplanned dialysis, and 10 studies adjusted for covariates in multivariable models to identify independent associations. Increased age, increased comorbidity burden, late referral to nephrology, and lower eGFR at dialysis initiation were the most common independent risk factors for unplanned dialysis. The published literature is limited by the retrospective, cross-sectional, and often unadjusted, confounded nature of the data, along with varying terminology and criteria used to define unplanned dialysis across studies.

In univariate, unadjusted analyses, a lower hemoglobin, lower serum albumin, higher serum phosphate, lower serum calcium, and lower eGFR at dialysis initiation were often more common in patients with unplanned dialysis starts. However, these characteristics were often not examined in adjusted analyses or did not always persist as risk factors in

multivariable analysis.^{2,3,6,15,23,24} The independent association of factors such as lower hemoglobin, calcium, or higher phosphate with unplanned dialysis is questionable, given that these characteristics may be surrogate markers for poor predialysis care or patient nonadherence, and were only measured once at dialysis initiation. Lower eGFR at dialysis initiation could be due to late referral, a higher rate of eGFR decline, or patient, physician, or system-related delays with respect to RRT preparation. The retrospective nature of the data makes it difficult to comment on the underlying reasons for observed associations.

Increased age was an independent risk factor in 4 studies following adjustment for comorbidity burden and late referral.^{2,3,5,31} This could be due to physician-related factors; nephrologists may delay discussions about dialysis with elderly patients due to the uncertainty of meaningful survival and quality of life benefits and the high competing risk of death.⁵⁴⁻⁶⁰ As well, the benefits of arteriovenous fistulas in elderly patients are uncertain; therefore, nephrologists may decide that initiation of hemodialysis with a CVC, if needed, is entirely appropriate.⁶¹⁻⁶³ For these reasons, labeling all dialysis starts with a CVC as unplanned is contentious. Increased age may be associated with unplanned dialysis primarily due to increased “planned” CVC use, but studies that included access criteria in the definition for unplanned dialysis did not differentiate between CVC insertions under planned, stable conditions in the outpatient setting versus urgent conditions during a hospitalization.^{2,3} Differentiating between planned, elective and urgent, unplanned CVC insertions could help to better delineate the association between age and unplanned dialysis. Another potential contributor to the association between increased age and unplanned dialysis could be that elderly patients are at increased risk for acute illnesses and acute kidney injury.⁶⁴

The study by Nadeau-Fredette et al²⁶ included only home hemodialysis patients and was the only study that reported younger age as an independent risk factor for unplanned dialysis. This discrepant result is likely due to the fact that home hemodialysis patients are not representative of the general dialysis population. The study by Nadeau-Fredette et al²⁶ also reported that patients with a failed transplant were more likely to have an unplanned dialysis start. This was not examined in other studies but is an interesting finding that suggests an important care gap in preparing patients with a failing transplant for dialysis. Increased comorbidity burden and congestive heart failure were reported as independent risk factors in three^{3,26,31} and two^{5,53} studies, respectively. This suggests that patients with multiple medical issues, poor cardiac function, and issues with volume overload may require RRT planning at higher levels of kidney function and closer follow-up. Late referral to nephrology was an independent risk factor in 5 studies.^{3-5,31,48} The definition of late referral varied in these studies from less than 3 months⁴⁸ to less than 12 months.³ This finding supports the complexity of optimal RRT preparation, which may be underappreciated by

both patients and physicians. Several studies found that follow-up in a dedicated predialysis clinic and the receipt of dialysis education were less common in patients with an unplanned dialysis start.^{2,15,23,24,26,38,39,48,49,53} These findings were mostly reported in univariate analysis, but suggest that specialized care and education can facilitate the difficult transition onto dialysis. The finding of diabetic nephropathy and nephrosclerosis being more common than genetic kidney disease or glomerulonephritis in patients with unplanned dialysis starts was mostly reported in univariate analyses and may be explained by the fact that patients with diabetic nephropathy and nephrosclerosis tend to be older and have more comorbidities.

A prior systematic review examined outcomes and costs associated with unplanned dialysis and included literature up to 2008. This previously published review by Mendelssohn et al⁷ included 8 European studies and found that unplanned dialysis was associated with increased morbidity and mortality, along with significant health care costs. Our review includes the 8 studies from the Mendelssohn et al review, along with 40 further studies, and is the first systematic review to summarize the published evidence on risk factors for unplanned dialysis.

Our review benefits from a comprehensive, broad search strategy with all methods clearly defined and prespecified. However, the conclusions of our review are limited for several reasons. Only 12 studies actually specified the determination of risk factors for unplanned dialysis as a study objective and none of these studies had prospective follow-up of patients with CKD.^{2-5,19,21,23,24,26,39,48,53} Due to the retrospective or cross-sectional nature of the published data, results are largely limited to one-time data collection at dialysis initiation and data collected as part of routine clinical care. As well, many studies did not perform adjusted or matched analyses. The variable terminology and criteria used to define unplanned dialysis makes comparisons across studies difficult. Some studies focused solely on dialysis initiations during a hospitalization or under acute circumstances while other studies also included dialysis initiations with a CVC in their definition of unplanned dialysis. As well, not all studies that included incident dialysis patients specified the exclusion of patients with AKI (without prior CKD) requiring dialysis (Table 1). Such patients would obviously require inpatient/urgent dialysis with a CVC but are not of interest when considering the issue of risk factors for planned versus unplanned dialysis. Finally, some studies were conducted more than 10 years ago, and practice patterns with respect to predialysis care and dialysis initiation have changed. In particular, national guidelines have adopted a delayed approach to dialysis initiation, largely based on the results of the Initiating Dialysis Early and Late (IDEAL) Trial.⁶⁵⁻⁶⁷ There may also be regional or country-specific practice patterns and patient population differences that are not fully captured by the published data, ie, there are very little data from the United States published on this topic.⁴

Conclusions

High-quality data on patient risk factors for unplanned dialysis are lacking. As a first step toward reducing the incidence of unplanned dialysis starts, well-designed studies to determine modifiable risk factors are needed. Potential modifiable factors could include the timing of RRT education and factors that impact patient adherence and decision-making. The lack of a consensus definition for unplanned dialysis makes research and quality improvement initiatives in this area more challenging.

Author Contributions

A.O.M., S.H., and A.A. contributed to conception and design of the study; A.O.M., S.H., A.A., K.S.B., and P.A.B. provided intellectual content of critical importance to the work described; A.O.M. and R.H. interpreted the data; R.H. and A.O.M. drafted the first version of the article and revisions; all authors read and approved the final version of the article.

Availability of Data and Materials

This study is a systematic review of previously published data and materials.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: K.S.B. reports the receipt of personal fees from the Ontario Renal Network unrelated to this work.

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Supplemental Material

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