Identifying individuals at risk of needing CKD associated medications in a European kidney disease cohort

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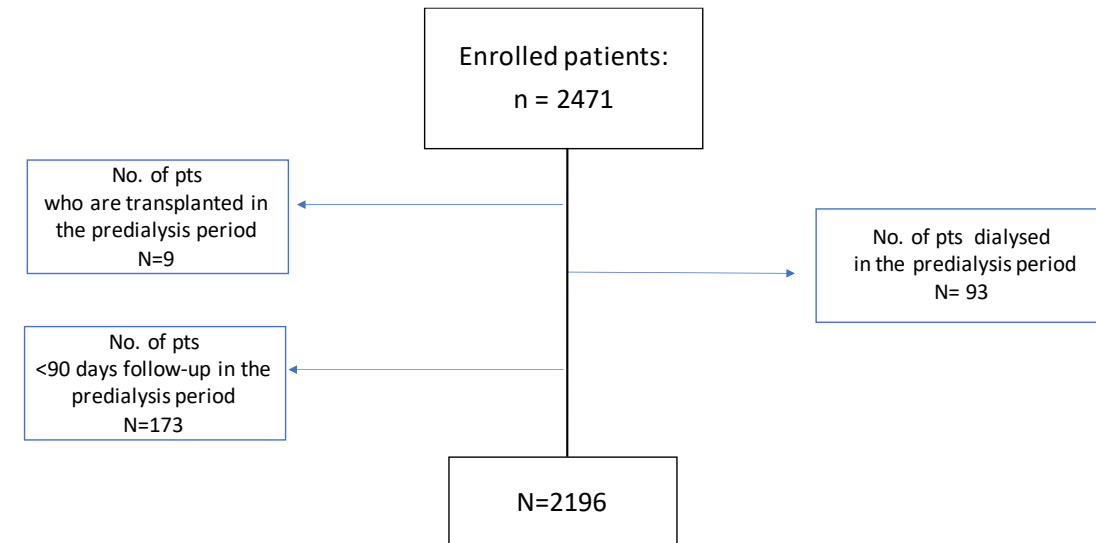
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Background

- Despite advances in care people on dialysis still face high mortality rates

- Suboptimal care during CKD stages G4/G5ND is a possible contributing factor

- Earlier specialized nephrology care before dialysis is associated with significantly better outcomes

- Anemia and CKD-MBD are modifiable risk factors for cardiovascular and kidney disease progression, emphasizing the need for early recognition and treatment.

  ➢ VDRA
  ➢ Phosphate binders
  ➢ ESAs
  ➢ Iron

Analyzing Data, recognizing Excellence and Optimizing Outcomes (ARO) cohort III

- Retrospective cohort of pre-haemodialysis patients enrolled in FMC

    - 1 Apr 2012 to 30 Jun 2014

    - Follow-up to 31 Dec 2016

- Inclusion/exclusion criteria:
  - Pre-haemodialysis patients CKD 4/5 aged ≥18
  - At least ≥90 days of follow-up

- Aro3 cohort by country:
  - ✓ Czech Republic
  - ✓ Italy
  - ✓ Russia
  - ✓ Serbia
  - ✓ Slovak Republic
  - ✓ Bosnia

Enrolled patients: n = 2471

No. of pts who are transplanted in the predialysis period N=9

No. of pts dialysed in the predialysis period N= 93

No. of pts <90 days follow-up in the predialysis period N=173

N=2196

Baseline Characteristics

Tables

Table 1. Baseline characteristics

	whole cohort (N=2196)	derivation cohort (N= 1440)	validation cohort (N=756)
Age at baseline (years)	69 ± 13	68.8 ± 13.2	69.2 ± 13.2
Gender			
Female	1138 (51.8)	745 (51.7)	393 (52.0)
Male	1058 (48.2)	695 (48.3)	363 (48.0)
Body mass index (kg/m²)	29 ± 5.9	29 ± 5.8	29.1 ± 6.0
missing	70 (3.2)	44 (3.0)	26 (3.4)
Smoking status			
Nonsmoker	1140 (51.9)	761 (52.8)	379 (50.1)
Former	430 (19.6)	275 (19.1)	155 (20.5)
Current	215 (9.8)	141 (9.8)	74 (9.8)
Missing	411 (18.7)	263 (18.3)	148 (19.6)
History of cancer	106 (4.8)	70 (4.9)	36 (4.8)
History of CVD	492 (22.4)	338 (23.5)	
History of diabetes	772 (35.2)	517 (35.9)	255 (33.7)
History of hypertension	1022 (46.5)	686 (47.6)	336 (44.4)
Chronic kidney disease etiology			
Hypertension/vascular	46 (21.7)	331 (23.0)	145 (19.2)
Glomerulonephritis	146 (6.6)	91 (6.3)	55 (7.3)
Diabetes	530 (24.1)	348 (24.2)	182 (24.1)
Tubulo-interstitial	347 (15.8)	224 (15.6)	123 (16.3)
Polycystic kidney disease	84 (3.8)	50 (3.5)	34 (4.5)
Miscellaneous/other	477 (21.7)	313 (21.7)	164 (21.7)
Missing	136 (6.2)	83 (5.8)	53 (7.0)
Country			
Italy	526 (24)	334 (23.2)	192 (25.4)
Czech Republic	706 (32.1)	465 (32.3)	241 (31.9)
Serbia	123 (5.6)	85 (5.9)	38 (5.0)
Bosnia	56 (2.5)	35 (2.4)	21 (2.8)
Slovak Republic	625 (28.5)	412 (28.6)	213 (28.2)
Russia	160 (7.3)	109 (7.6)	51 (6.7)
Iron at referral	385 (17.5)	251 (17.4)	134 (17.7)
ESA at referral	285 (13.0)	189 (13.1)	96 (12.7)
VDRA therapy at referral	611 (27.8)	401 (27.8)	210 (27.8)
Phosphate binders at referral	287 (13.1)	189 (13.1)	98 (13.0)
Amount of antihypertensives at referral			
0	989 (45.0)	646 (44.9)	343 (45.4)
1-2	1086 (49.5)	707 (49.1)	379 (50.1)
More than 3	121 (5.4)	87 (6.1)	34 (4.5)
RAS blockers at referral	739 (33.7)	484 (33.6)	255 (33.7)
Diuretic at referral	1133 (51.6)	756 (52.5)	377 (49.9)
Hemoglobin(g/l)	116 ± 16	116.2 ± 16	116.9 ± 16.8
Missing	186 (8.5)	116 (8.0)	70 (9.3)
Ferritin (µg/l)	276 (139, 524)	271 (142, 504)	280 (136,564)
Missing	822 (37.4)	544 (37.8)	278 (36.8)
Transferrin saturation (TSAT)	20.3 (15, 26)	20.0 (15, 26)	21(15, 27)
Missing	1315 (60.0)	860 (60.0)	455 (60.2)
Serum albumin (g/l)	40.6 ± 4.4	40.5 ± 4.5	40.6 ± 4.4
Missing	482 (21.9)	308 (21.4)	174 (23.0)
Total calcium(mmol/l)	2.3 ± 0.18	2.3 ± 0.18	2.3 ± 0.18
Missing	273 (12.4)	184 (12.8)	89 (11.8)
Phosphate (mmol/l)	1.3 ± 0.29	1.3 ± 0.28	1.3 ± 0.3
Missing	285 (13.0)	189 (13.0)	96 (12.7)
iPTH (ng/l)	124 (72, 202)	125 (73, 201)	121 (72, 206)
Missing	479 (21.8)	321 (22.3)	158 (20.9)
eGFR (CKD-EPI)	18.6 ± 6.5	18.5 ± 6.5	18.8 ± 6.5
Missing	243 (11.0)	156 (10.8)	87 (11.5)
Days of follow-up	735 (290, 1255)	733 (293, 1264)	752 (283, 1237)

- Mean age: 69 years old
- 52% women
- Diabetic nephropathy followed by hypertensive nephropathy were the most common causes of CKD.
- eGFR at baseline: 18.6 ml/min/1.73m^2.
- Derivation and Validation cohort: no significant differences and shared similar traits with the entire cohort.

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Risk of requiring CKD-related pharmacotherapy

Table 2. Multivariate logistic regression of the risk of requiring CKD-related pharmacotherapy during the pre-dialysis period

Risk for requiring ESAs during the pre-dialysis period.

	P value	OR[1] (95% CI)
VDRA at referral	0.052	1.61 (0.99-2.60)
Iron at referral	0.042	1.85 (1.02-3.35)
eGFR at referral	0.026	0.95 (0.92-0.99)
Hemoglobin ref. < 100 g/l	0.053	2.24 (0.99-4.60)
Hemoglobin ref. 100- 120 g/l	0.040	2.18(1.28-3.71)
iPTH ref. > 150 ng/l	0.044	1.66(1.01-2.73)

Risk for requiring iron therapy during the pre-dialysis period.

	P value	OR[1] (95% CI)
eGFR ref. (CKD-EPI)	<0.001	0.93 (0.89-0.97)
ESAs at referral	0.058	2.02 (0.98-4.17)

Risk for requiring phosphate binders during the pre-dialysis period.

	P value	OR[1] (95% CI)
Age > 80	0.03	0.20 (0.07-0.58)
Age 50-60	0.09	0.47 (0.18-1.15)
Age 61-70	0.08	0.33 (0.15-0.75)
Age 71-80	0.02	0.28 (0.13-0.64)
iPTH ref. > 150 ng/l	0.03	2.33 (1.33-4.04)
Hemoglobin ref. < 100 g/l	0.009	2.75 (1.29-5.86)
Hemoglobin ref. 100- 120 g/l	0.70	1.13 (0.6-2.09)
Serum albumin > 35 g/l	0.01	2.46 (1.29-5.86)
eGFR ref. (CKD-EPI)	0.05	0.93 (0.90-0.98)

Risk for requiring VDRA during the pre-dialysis period

	P value	OR[1] (95% CI)
History of infections	0.066	3.87 (0.913-16.375)
History of diabetes	0.025	1.55 (1.06-4.77)
Serum albumin > 35 g/l	0.016	2.40 (1.18-4.91)
Calcium < 2.1 mmol/l	0.189	1.54 (0.81-2.93)
Calcium > 2.6 mmol/l	0.040	2.27 (1.04-4.96)
iPTH > 150 ng/l	< 0.001	3.2 (2.15-4.77)

Table 3. C-statistic for the models predicting CKD-related pharmacotherapy

	Area	95% CIs
ESAs		
Derivation cohort	0.700	0.643-0.750
Validation cohort	0.728	0.652-0.803
Iron		
Derivation cohort	0.641	0.568-0.713
Validation cohort	0.630	0.545-0.715
Phosphate binders		
Derivation cohort	0.732	0.667-0.797
Validation cohort	0.741	0.663-0.819
VDRA		
Derivation cohort	0.659	0.619-0.716
Validation cohort	0.668	0.590-0.729

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Conclusion

- Age, history of diabetes, iPTH, hemoglobin, calcium and serum albumin levels predicted medication needs.

- The models showed varying prediction capabilities, which were best for ESAs and phosphate binders.

- **16% of patients were predicted to have a likelihood of receiving any of these medications of less than 20%.**

- By identifying low-risk patients who may require less frequent follow-up the study has the potential to optimize the use of healthcare resources and enhance patient care.

- This holistic approach could lead to more individualized and effective management of CKD-related complications, ultimately benefiting both patients and healthcare systems.