Supplemental Material

Urinary Angiotensinogen and Progression of Chronic Kidney Disease: Results from KNOW-CKD Study

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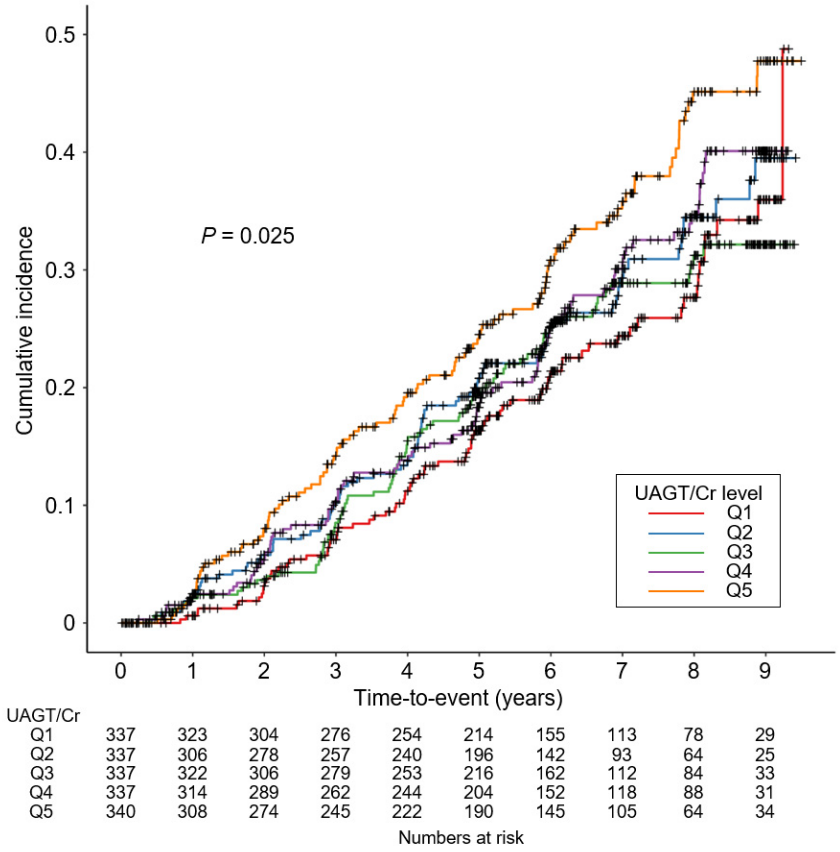

Figure S1. Kaplan-Meier survival curve for cumulative incidence of decline of kidney function by UAGT/Cr.

Note: *P* value by Log-rank test. Abbreviations: Q1, 1st quintile; Q2, 2nd quintile, Q3, 3rd quintile; Q4, 4th quintile; Q5, 5th quintile; UAGT/Cr, urinary angiotensinogen-to-creatinine ratio.

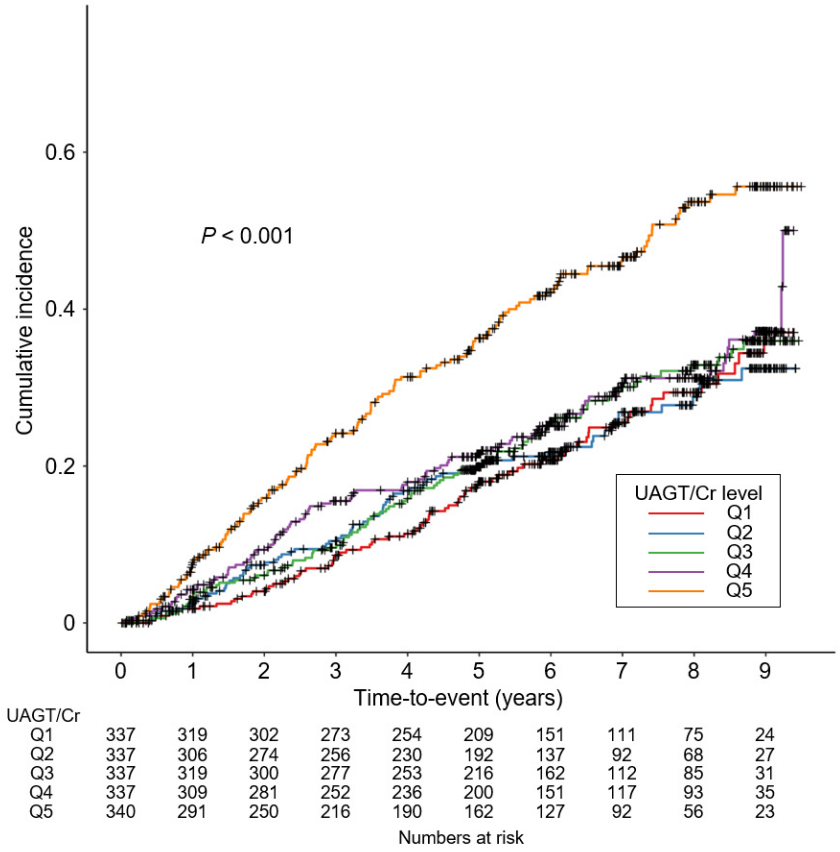

Figure S2. Kaplan-Meier survival curve for cumulative incidence of onset of ESRD by UAGT/Cr.

Note: *P* value by Log-rank test. Abbreviations: Q1, 1st quintile; Q2, 2nd quintile, Q3, 3rd quintile; Q4, 4th quintile; Q5, 5th quintile; UAGT/Cr, urinary angiotensinogen-to-creatinine ratio.

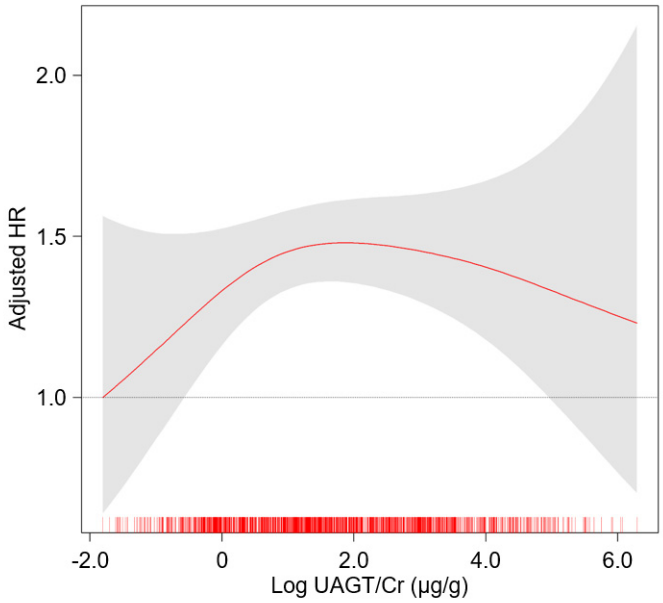

Figure S3. Restricted cubic spline of UAGT/Cr on decline of kidney function.

Note: Adjusted HR of UAGT/Cr as a continuous variable for composite renal event is depicted. The model was adjusted for age, sex, age-adjusted Charlson comorbidity index, primary renal disease, current smoking, medications (ACEi/ARBs, diuretics, number of antihypertensive drugs, statins), BMI, SBP, DBP, hemoglobin, albumin, fasting glucose, total cholesterol, LDL-C, HDL-C, TG, 25(OH) vitamin D, hs-CRP, serum creatinine and spot urine ACR.

Abbreviations: HR, hazard ratio; UAGT/Cr, urinary angiotensinogen-to-creatinine ratio.

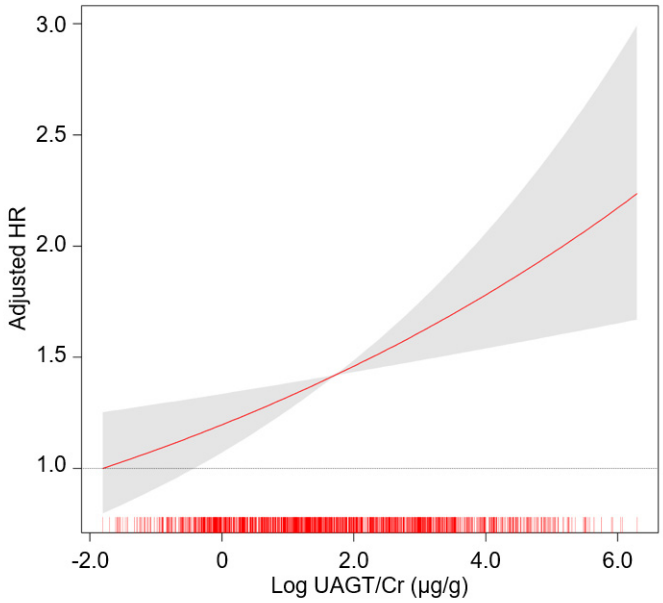

Figure S4. Restricted cubic spline of UAGT/Cr on onset of ESRD.

Note: Adjusted HR of UAGT/Cr as a continuous variable for composite renal event is depicted. The model was adjusted for age, sex, age-adjusted Charlson comorbidity index, primary renal disease, current smoking, medications (ACEi/ARBs, diuretics, number of antihypertensive drugs, statins), BMI, SBP, DBP, hemoglobin, albumin, fasting glucose, total cholesterol, LDL-C, HDL-C, TG, 25(OH) vitamin D, hs-CRP, serum creatinine and spot urine ACR.

Abbreviations: HR, hazard ratio; UAGT/Cr, urinary angiotensinogen-to-creatinine ratio.

Table S1. HRs for decline of kidney function by UAGT/Cr level.

	UAGT/Cr	Events, n (%)	Model 1		Model 2		Model 3		Model 4	
			HR (95%CIs)	*P* value	HR (95%CIs)	*P* value	HR (95%CIs)	*P* value	HR (95%CIs)	*P* value
Decline of kidney function	Q1	77 (22.8)	Reference		Reference		Reference		Reference	
	Q2	84 (24.9)	1.177 (0.844, 1.641)	0.338	1.384 (1.013, 1.891)	0.414	1.391 (0.991, 1.954)	0.056	1.402 (0.997, 1.972)	0.052
	Q3	84 (24.9)	1.060 (0.764, 1.473)	0.726	1.278 (0.931, 1.753)	0.129	1.309 (0.935, 1.832)	0.117	1.317 (0.939, 1.848)	0.111
	Q4	91 (27.0)	1.345 (0.978, 1.848)	0.068	1.245 (0.913, 1.699)	0.166	1.313 (0.943, 1.827)	0.106	1.284 (0.918, 1.795)	0.144
	Q5	108 (31.8)	1.632 (1.195, 2.228)	0.002	1.375 (1.019, 1.856)	0.037	1.309 (0.945, 1.814)	0.105	1.204 (0.858, 1.691)	0.283

Note: Model 1, unadjusted model. Model 2, model 1 + adjusted for age, sex, age-adjusted Charlson comorbidity index, primary renal disease, current smoking, medication (ACEi/ARBs, diuretics, number of antihypertensive drugs, statins), BMI, SBP and DBP. Model 3, model 2 + adjusted for hemoglobin, albumin, total cholesterol, LDL-C, HDL-C, TG, fasting glucose, 25(OH) vitamin D, and, hs-CRP. Model 4, model 3 + serum creatinine and spot urine ACR. Abbreviations: CI, confidence interval; HR, hazard ratio; Q1, 1st quintile; Q2, 2nd quintile, Q3, 3rd quintile; Q4, 4th quintile; Q5, 5th quintile; UAGT/Cr, urinary angiotensinogen-to-creatinine ratio.

Table S2. HRs for onset of ESRD by UAGT/Cr level.

	UAGT/Cr	Events, n (%)	Model 1		Model 2		Model 3		Model 4	
			HR (95%CIs)	*P* value	HR (95%CIs)	*P* value	HR (95%CIs)	*P* value	HR (95%CIs)	*P* value
Onset of ESRD	Q1	77 (22.8)	Reference		Reference		Reference		Reference	
	Q2	74 (22.0)	1.003 (0.712, 1.413)	0.987	1.208 (0.875, 1.668)	0.250	1.256 (0.887, 1.780)	0.199	0.831 (0.565, 1.224)	0.349
	Q3	91 (27.0)	1.152 (0.837, 1.587)	0.385	1.574 (1.153, 2.148)	0.004	1.562 (1.120, 2.178)	0.009	1.470 (1.054, 2.049)	0.023
	Q4	94 (27.9)	1.368 (0.995, 1.866)	0.053	1.480 (1.008, 2.013)	0.013	1.568 (1.133, 2.171)	0.007	1.336 (0.963, 1.852)	0.083
	Q5	142 (41.8)	2.282 (1.700, 3.063)	< 0.001	2.006 (1.508, 2.668)	< 0.001	1.901 (1.390, 2.600)	< 0.001	1.444 (1.050, 1.987)	0.024

Note: Model 1, unadjusted model. Model 2, model 1 + adjusted for age, sex, age-adjusted Charlson comorbidity index, primary renal disease, current smoking, medication (ACEi/ARBs, diuretics, number of antihypertensive drugs, statins), BMI, SBP and DBP. Model 3, model 2 + adjusted for hemoglobin, albumin, total cholesterol, LDL-C, HDL-C, TG, fasting glucose, 25(OH) vitamin D, and, hs-CRP. Model 4, model 3 + serum creatinine and spot urine ACR. Abbreviations: CI, confidence interval; ESRD, end-stage renal disease; HR, hazard ratio; Q1, 1st quintile; Q2, 2nd quintile, Q3, 3rd quintile; Q4, 4th quintile; Q5, 5th quintile; UAGT/Cr, urinary angiotensinogen-to-creatinine ratio.

Table S3. HRs for composite renal event by UAGT/Cr level after excluding the subjects at CKD stage 1.

	UAGT/Cr	Events, n (%)	Model 1		Model 2		Model 3		Model 4	
			HR (95%CIs)	*P* value	HR (95%CIs)	*P* value	HR (95%CIs)	*P* value	HR (95%CIs)	*P* value
Composite renal event	Q1	101 (36.1)	Reference		Reference		Reference		Reference	
	Q2	107 (39.5)	1.277 (0.952, 1.712)	0.103	1.444 (1.070, 1.948)	0.016	1.465 (1.112, 1.929)	0.007	1.152 (0.837, 1.586)	0.385
	Q3	111 (42.4)	1.256 (0.944, 1.673)	0.118	1.440 (1.071, 1.936)	0.016	1.453 (1.010, 1.918)	0.008	1.403 (1.043, 1.888)	0.025
	Q4	120 (44.3)	1.495 (1.132, 1.975)	0.005	1.508 (1.127, 2.016)	0.006	1.487 (1.132, 1.952)	0.004	1.289 (0.961, 1.730)	0.090
	Q5	175 (56.8)	2.225 (1.713, 2.892)	< 0.001	1.804 (1.361, 2.390)	< 0.001	1.966 (1.526, 2.533)	< 0.001	1.449 (1.087, 1.932)	0.012

Note: Model 1, unadjusted model. Model 2, model 1 + adjusted for age, sex, age-adjusted Charlson comorbidity index, primary renal disease, current smoking, medication (ACEi/ARBs, diuretics, number of antihypertensive drugs, statins), BMI, SBP and DBP. Model 3, model 2 + adjusted for hemoglobin, albumin, total cholesterol, LDL-C, HDL-C, TG, fasting glucose, 25(OH) vitamin D, and, hs-CRP. Model 4, model 3 + serum creatinine and spot urine ACR. Abbreviations: CI, confidence interval; HR, hazard ratio; Q1, 1st quintile; Q2, 2nd quintile, Q3, 3rd quintile; Q4, 4th quintile; Q5, 5th quintile; UAGT/Cr, urinary angiotensinogen-to-creatinine ratio.

Table S4. HRs for composite renal event by UAGT/Cr level after excluding the subjects at CKD stage 5.

	UAGT/Cr	Events, n (%)	Model 1		Model 2		Model 3		Model 4	
			HR (95%CIs)	*P* value	HR (95%CIs)	*P* value	HR (95%CIs)	*P* value	HR (95%CIs)	*P* value
Composite renal event	Q1	96 (29.4)	Reference		Reference		Reference		Reference	
	Q2	102 (31.5)	1.204 (0.891, 1.627)	0.226	1.440 (1.086, 1.910)	0.011	1.564 (1.150, 2.128)	0.004	1.397 (1.204, 1.907)	0.035
	Q3	100 (30.9)	1.063 (0.781, 1.419)	0.734	1.346 (1.009, 1.795)	0.042	1.450 (1.064, 1.975)	0.019	1.241 (0.906, 1.698)	0.179
	Q4	110 (34.9)	1.389 (1.041, 1.855)	0.026	1.458 (1.101, 1.931)	0.009	1.653 (1.223, 2.233)	0.001	1.288 (0.944, 1.756)	0.110
	Q5	143 (48.0)	2.164 (1.640, 2.854)	< 0.001	1.868 (1.433, 2.434)	< 0.001	1.861 (1.389, 2.495)	< 0.001	1.444 (1.069, 1.951)	0.017

Note: Model 1, unadjusted model. Model 2, model 1 + adjusted for age, sex, age-adjusted Charlson comorbidity index, primary renal disease, current smoking, medication (ACEi/ARBs, diuretics, number of antihypertensive drugs, statins), BMI, SBP and DBP. Model 3, model 2 + adjusted for hemoglobin, albumin, total cholesterol, LDL-C, HDL-C, TG, fasting glucose, 25(OH) vitamin D, and, hs-CRP. Model 4, model 3 + serum creatinine and spot urine ACR. Abbreviations: CI, confidence interval; HR, hazard ratio; Q1, 1st quintile; Q2, 2nd quintile, Q3, 3rd quintile; Q4, 4th quintile; Q5, 5th quintile; UAGT/Cr, urinary angiotensinogen-to-creatinine ratio.

Table S5. HRs for composite renal event by UAGT/Cr level after excluding the subjects with DM.

	UAGT/Cr	Events, n (%)	Model 1		Model 2		Model 3		Model 4	
			HR (95%CIs)	*P* value	HR (95%CIs)	*P* value	HR (95%CIs)	*P* value	HR (95%CIs)	*P* value
Composite renal event	Q1	62 (25.2)	Reference		Reference		Reference		Reference	
	Q2	69 (25.9)	1.136 (0.785, 1.644)	0.498	1.433 (1.009, 2.034)	0.044	1.515 (1.033, 2.224)	0.034	1.164 (0.773, 1.753)	0.466
	Q3	79 (29.5)	1.222 (0.860, 1.735)	0.264	1.429 (1.015, 2.012)	0.040	1.575 (1.093, 2.269)	0.015	1.515 (1.052, 2.182)	0.026
	Q4	81 (30.2)	1.364 (0.963, 1.931)	0.080	1.221 (0.870, 1.716)	0.249	1.464 (1.019, 2.104)	0.039	1.240 (0.860, 1.786)	0.249
	Q5	111 (48.9)	2.526 (1.814, 3.518)	< 0.001	2.117 (1.158, 2.913)	< 0.001	2.265 (1.602, 3.204)	< 0.001	1.901 (1.335, 2.707)	< 0.001

Note: Model 1, unadjusted model. Model 2, model 1 + adjusted for age, sex, age-adjusted Charlson comorbidity index, primary renal disease, current smoking, medication (ACEi/ARBs, diuretics, number of antihypertensive drugs, statins), BMI, SBP and DBP. Model 3, model 2 + adjusted for hemoglobin, albumin, total cholesterol, LDL-C, HDL-C, TG, fasting glucose, 25(OH) vitamin D, and, hs-CRP. Model 4, model 3 + serum creatinine and spot urine ACR. Abbreviations: CI, confidence interval; HR, hazard ratio; Q1, 1st quintile; Q2, 2nd quintile, Q3, 3rd quintile; Q4, 4th quintile; Q5, 5th quintile; UAGT/Cr, urinary angiotensinogen-to-creatinine ratio.

Table S6. HRs for composite renal event by UAGT/Cr level after excluding the subjects with PKD.

	UAGT/Cr	Events, n (%)	Model 1		Model 2		Model 3		Model 4	
			HR (95%CIs)	*P* value	HR (95%CIs)	*P* value	HR (95%CIs)	*P* value	HR (95%CIs)	*P* value
Composite renal event	Q1	90 (31.2)	Reference		Reference		Reference		Reference	
	Q2	97 (37.2)	1.358 (0.996, 1.852)	0.053	1.483 (1.084, 2.028)	0.014	1.519 (1.106, 2.086)	0.010	1.160 (0.829, 1.625)	0.386
	Q3	94 (35.7)	1.182 (0.868, 1.608)	0.289	1.489 (1.088, 2.038)	0.013	1.456 (1.059, 2.003)	0.021	1.360 (0.989, 1.871)	0.058
	Q4	108 (38.4)	1.424 (1.060, 1.913)	0.019	1.623 (1.200, 2.196)	0.002	1.576 (1.159, 2.141)	0.004	1.257 (0.923, 1.713)	0.147
	Q5	155 (51.8)	2.179 (1.650, 2.877)	< 0.001	2.125 (1.595, 2.831)	< 0.001	1.844 (1.374, 2.475)	< 0.001	1.363 (1.009, 1.841)	0.044

Note: Model 1, unadjusted model. Model 2, model 1 + adjusted for age, sex, age-adjusted Charlson comorbidity index, primary renal disease, current smoking, medication (ACEi/ARBs, diuretics, number of antihypertensive drugs, statins), BMI, SBP and DBP. Model 3, model 2 + adjusted for hemoglobin, albumin, total cholesterol, LDL-C, HDL-C, TG, fasting glucose, 25(OH) vitamin D, and, hs-CRP. Model 4, model 3 + serum creatinine and spot urine ACR. Abbreviations: CI, confidence interval; HR, hazard ratio; Q1, 1st quintile; Q2, 2nd quintile, Q3, 3rd quintile; Q4, 4th quintile; Q5, 5th quintile; UAGT/Cr, urinary angiotensinogen-to-creatinine ratio.

Table S7. HRs for composite renal event by UAGT/Cr level in the quartile division.

	UAGT/Cr	Events, n (%)	Model 1		Model 2		Model 3		Model 4	
			HR (95%CIs)	*P* value	HR (95%CIs)	*P* value	HR (95%CIs)	*P* value	HR (95%CIs)	*P* value
Composite renal event	1st quarter	132 (31.3)	Reference		Reference		Reference		Reference	
	2nd quarter	152 (36.0)	1.187 (0.924, 1.524)	0.179	1.381 (1.089, 1.751)	0.008	1.325 (1.026, 1.711)	0.031	1.111 (0.851, 1.449)	0.440
	3rd quarter	136 (32.2)	1.072 (0.834, 1.377)	0.589	1.247 (0.976, 1.594)	0.078	1.337 (1.030, 1.734)	0.029	1.148 (0.883, 1.491)	0.303
	4th quarter	212 (50.2)	2.050 (1.629, 2.580)	< 0.001	1.781 (1.424, 2.228)	< 0.001	1.758 (1.378, 2.244)	< 0.001	1.385 (1.078, 1.778)	0.011

Note: Model 1, unadjusted model. Model 2, model 1 + adjusted for age, sex, age-adjusted Charlson comorbidity index, primary renal disease, current smoking, medication (ACEi/ARBs, diuretics, number of antihypertensive drugs, statins), BMI, SBP and DBP. Model 3, model 2 + adjusted for hemoglobin, albumin, total cholesterol, LDL-C, HDL-C, TG, fasting glucose, 25(OH) vitamin D, and, hs-CRP. Model 4, model 3 + serum creatinine and spot urine ACR. Abbreviations: CI, confidence interval; HR, hazard ratio; UAGT/Cr, urinary angiotensinogen-to-creatinine ratio.

Table S8. HRs for composite renal event by UAGT/Cr level, where the co-variate 'serum creatinine level' was replaced with 'eGFR'.

	UAGT/Cr	Adjusted	
		HR (95%CIs)	*P* value
Composite renal event	Q1	Reference	
	Q2	1.278 (0.948, 1.724)	0.108
	Q3	1.286 (0.958, 1.726)	0.095
	Q4	1.197 (0.892, 1.604)	0.230
	Q5	1.427 (1.078, 1.888)	0.013

Note: Adjusted for age, sex, age-adjusted Charlson comorbidity index, primary renal disease, current smoking, medication (ACEi/ARBs, diuretics, number of antihypertensive drugs, statins), BMI, SBP, DBP, hemoglobin, albumin, total cholesterol, LDL-C, HDL-C, TG, fasting glucose, 25(OH) vitamin D, hs-CRP, eGFR and spot urine ACR. Abbreviations: CI, confidence interval; HR, hazard ratio; Q1, 1st quintile; Q2, 2nd quintile, Q3, 3rd quintile; Q4, 4th quintile; Q5, 5th quintile; UAGT/Cr, urinary angiotensinogen-to-creatinine ratio.