Kidney Biopsy-related Complications in Hospitalized Patients with Acute Kidney Disease

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Supplementary Table 1. Transfusion and death adjudication details

Patient study identifier	Patient risk factors							Complications				Biopsy-related	Adjudication notes
	Age	Sex	Hgb	Plt.	BUN	Creat.	Diag.	Trans-fusion	Interv-ention	Death	Hematoma		
01-0117	45	F	8	120	24	3.9	MPGN	Yes	Yes	No	Medium or large	Yes	Hematoma and required intervention.
01-0156	46	F	8.8	100	120	3.2	Inadequate	Yes	Yes	No	Medium or large	Yes	Transfusion in IR while embolization of pseudo-aneurysms was completed post-biopsy.
01-0204	57	M	9.3	183	88	3.0	ATN	Yes	Yes	No	Medium or large	Yes	Full dose anticoagulation started within 24 hours of biopsy; large hematoma on CT; required coiling.
01-0254	49	M	9.4	50	91	4.6	ATN	Yes	No	Yes	Medium or large	Yes	Death was not due to kidney biopsy. Autopsy showed miliary TB, schistosomiasis, hemophagocytic lymphohistiocytosis.
01-0010	80	F	6.9	309	61	3.8	ANCA	Yes	No	No	Medium or large	Yes	Ipsilateral hematoma from biopsy.
01-0017	26	F	8.5	194	59	5.2	ATN	Yes	No	No	Small	Yes	Ipsilateral hematoma after biopsy; patient with cirrhosis; low hemoglobin before biopsy.
01-0072	37	F	7.3	87	54	1.4	FSGS	Yes	No	No	Absent	Yes	Likely combination of blood loss, iron deficiency and anemia of chronic disease.
01-0082	66	F	7.5	244	60	6.9	ATN	Yes	No	No	Medium or large	Yes	Possibly related; 5 cm hematoma after biopsy, but only a slight drop in Hb (8-->7) and transfused per protocol.
01-0177	54	F	8.5	84	38	2.2	DKD	Yes	No	No	Small	Yes	Hematoma after biopsy; was restarted on pradaxa after biopsy.
01-0181	73	M	6.9	103	155	18.4	Other	Yes	No	No	Medium or large	Yes	Large RP hematoma.
01-0230	76	F	8.4	122	155	9.7	Other	Yes	No	No	Medium or large	Yes	RP bleed on CT scan. Was started on heparin immediately after biopsy for suspected APLS.
01-0259	61	F	8.6	69	70	8.3	FSGS	Yes	No	No	Medium or large	Yes	Large hematoma on CT.
01-0077	59	M	7.5	94	46	2.1	Lupus	Yes	No	No	Medium or large	No	Intra-abdominal bleed believed to be unrelated to liver/kidney biopsies.
01-0018	43	F	8.6	228	40	6.1	Other	No	No	No	Medium or large	N/A	Not applicable
01-0133	64	F	9.2	388	63	1.8	ANCA	No	No	No	Medium or large	N/A	Not applicable
01-0027	83	M	10.5	289	63	3.4	FSGS	Yes	No	Yes	Small	No	Right sided bleed (left was biopsied). Patient with critical limb ischemia, septic shock, hepatocellular carcinoma-death not related to biopsy.
01-0236	46	F	9.3	162	76	3.4	ATN	Yes	No	Yes	Absent	No	Transfused 1 week after biopsy in the setting of ARDS and hypotension. Unrelated to biopsy. Patient with decompensated cirrhosis in MICU with ARDS, septic shock, and AKI. Death unrelated to biopsy.

01-0031	60	F	9.4	381	146	14.8	ANCA	Yes	No	No	Absent	No	Transfusion for apheresis.
01-0043	74	M	8.1	141	41	1.2	FSGS	Yes	No	No	Absent	No	Transfusion due to anemia from CMML.
01-0056	69	F	8.1	709	46	2.6	ANCA	Yes	No	No	Absent	No	Autoimmune hemolytic anemia.
01-0100	65	M	7	47	56	8.1	ATN	Yes	No	No	Absent	No	Patient with multiple myeloma. No hematoma.
01-0121	77	M	8.9	444	36	1.5	IgA	Yes	No	No	Absent	No	No hematoma, patient with colitis in intensive care unit.
01-0152	73	M	7.9	157	119	3.8	ANS	Yes	No	No	Small	No	Steady decline in Hb likely secondary to marrow hypo-activity.
01-0158	51	M	7.4	168	71	3.1	ATN	Yes	No	No	Absent	No	Transfused per protocol, no hematoma.
01-0161	67	M	7.4	92	30	2.4	AIN	Yes	No	No	Absent	No	No hematoma.
01-0165	54	M	7.3	64	64	3.1	IgA	Yes	No	No	Absent	No	Anemia attributed to slow intermittent GIB; no hematoma on imaging.
01-0171	51	M	7.6	430	31	6.4	ANS	Yes	No	No	Absent	No	Chronic anemia; no hematoma.
01-0172	37	F	7.5	49	48	6.9	Other	Yes	No	No	Not checked	No	Anemia likely due to group mismatched transfusion.
01-0202	55	M	7.1	624	54	6.8	AIN	Yes	No	No	Small	No	Anemia before biopsy, transfused per protocol. Tiny hematoma after biopsy.
01-0222	61	F	6.8	104	56	9.3	Other	Yes	No	No	Absent	No	Multiple myeloma; no hematoma.
01-0252	65	M	7.7	168	21	2.3	ATN	Yes	No	No	Absent	No	No hematoma.
01-0258	64	F	8.5	151	27	3.4	ATN	Yes	No	No	Absent	No	No hematoma.
01-0268	66	M	7.9	456	40	2.8	IgA	Yes	No	No	Small	No	Tiny hematoma with minimal drop in Hb; patient with MDS requiring chronic transfusions.
01-0269	29	M	8.4	285	46	3.4	DKD	Yes	No	No	Small	No	Small hematoma.
02-0025	74	M	9.8	129	36	6.6	ANS	Yes	No	No	Absent	No	Transfusion 1 week after biopsy; no hematoma.
02-0040	81	M	9.1	199	65	4.4	ANCA	Yes	No	No	Absent	No	Anemia likely secondary to chronic inflammation; no hematoma on CT.
01-0098	82	M	9.2	125	67	4.9	Other	No	No	Yes	Absent	No	Patient with decompensated cirrhosis who developed GI bleed and septic shock 17 days after biopsy. Death was unrelated to biopsy.

Age is expressed in years, sex as M (Male) or F (Female), hemoglobin (Hgb) level and platelet count (Plt) before biopsy in g/dl and 1000/mm^3, respectively, and blood urea nitrogen (BUN) and creatinine (creat) at biopsy in mg/dl. Diagnoses (diag.) are listed as membranoproliferative glomerulonephritis (MPGN), acute tubular necrosis/injury (ATN), acute interstitial nephritis (AIN), anti-neutrophil cytoplasmic antibody-associate vasculitis (ANCA), focal segmental glomerulosclerosis (FSGS), diabetic kidney disease (DKD), IgA Nephropathy (IgA) and arterionephrosclerosis (ANS).

Supplementary Table 2. ICD-9 procedure and diagnosis codes used in this study

Diagnosis	Codes	Description of procedure or diagnosis
Kidney biopsy	5523	Closed [percutaneous] [needle] biopsy of kidney
Transfusions	V582	Blood transfusion, without reported diagnosis
	9903	Other transfusion of whole blood
	9904	Transfusion of packed cells
Angiographic interventions	8845	Arteriography of renal arteries
	0025	Intravascular imaging of renal vessels
Hematoma	99812	Hematoma complicating a procedure
	86601	Injury to kidney without mention of open wound into cavity, hematoma without rupture of capsule
Acute Kidney Injury	5845	Acute kidney failure with lesion of tubular necrosis
	5846	Acute kidney failure with lesion of renal cortical necrosis
	5847	Acute kidney failure with lesion of renal medullary [papillary] necrosis
	5848	Acute kidney failure with other specified pathological lesion in kidney
	5849	Acute kidney failure, unspecified
Renal malignancy	1890	Malignant neoplasm of kidney, except pelvis
	1891	Malignant neoplasm of renal pelvis
	1980	Secondary malignant neoplasm of kidney
	20924	Malignant carcinoid tumor of the kidney
	20964	Benign carcinoid tumor of the kidney
	2230	Benign neoplasm of kidney, except pelvis
	2231	Benign neoplasm of renal pelvis
	23691	Neoplasm of uncertain behavior of kidney and ureter
Transplant	V420	Kidney replaced by transplant
	99681	Complications of transplanted kidney

Supplementary Table 3. Univariable association of risk factors with complications in hospitalized patients with acute kidney disease

Characteristic	Complication*	No complication	P-value*
N	15	144	
Demographics			
Age, years	58 (45, 67)	59 (49, 69)	0.66
Female	11 (73%)	56 (39%)	0.01
Black race	5 (33%)	31 (22%)	0.31
Diabetes	2 (14%)	61 (43%)	0.04
Hypertension	9 (60%)	96 (67%)	0.58
Cirrhosis	3 (21%)	17 (12%)	0.31
Chronic kidney disease	8 (53%)	83 (63%)	0.45
Body mass index (BMI), kg/m2	26 (24, 31)	28 (25, 33)	0.39
BMI>35kg/m2	2 (13%)	29 (20%)	0.52
Baseline Laboratory Features			.
Baseline Creatinine, mg/dl	1.1 (0.8, 1.6)	1.3 (1.0, 2.0)	0.33
Baseline GFR, ml/min	55 (33, 69)	45 (29, 74)	0.65
Baseline Protein to creatinine ratio, mg/mg	1.7 (1.3, 5.7)	2.3 (0.5, 5.1)	0.68
Dipstick protein ≥3+	14 (93%)	96 (70%)	0.06
Features at Biopsy			.
Acute kidney injury (AKI)	12 (80%)	119 (83%)	0.75
Stage 1	8 (53%)	72 (51%)	
Stage 2 or higher	3 (20%)	38 (27%)	
Dialysis	3 (20%)	13 (9%)	
Acute kidney disease (excluding AKI)	3 (20%)	24 (17%)	0.75
Creatinine, mg/dl	5.7 (2.3, 8.3)	4.4 (3.2, 6.4)	0.48
Blood Urea Nitrogen, mg/dl	61 (46, 91)	51 (34, 76)	0.07
BUN>60 mg/dl	9 (60%)	56 (39%)	0.12
Hemoglobin, g/dl	8.5 (7.5, 8.8)	9.4 (8.1, 10.5)	0.003
Hemoglobin<10 g/dl	15 (100%)	100 (70%)	0.01
Platelets per mm^3	120 (87, 228)	209 (151, 285)	0.008
Location			0.05
Floor	11 (73%)	131 (92%)	
Intensive care unit	4 (27%)	12 (8%)	
York Street campus (vs. St. Raphael's campus)	15 (100%)	112 (78%)	0.04
Procedural Factors			.
Passes	3 (2, 3)	2 (3, 3)	0.95
Fellow (vs. Attending)	14 (93%)	85 (61%)	0.01
Nephrology (vs. Radiology)	14 (93%)	89 (63%)	0.02
Needle Gauge 16 (vs. 18)	12 (80%)	76 (53%)	0.05
Ultrasound-guided (vs. CT)	14 (93%)	104 (73%)	0.08
Post-procedural findings and complications			
Hemoglobin after biopsy	6.7 (6.3, 7.1)	8.4 (7.5, 9.5)	<0.001
Drop in hemoglobin	1.3 (0.7, 2.0)	0.7 (0.3, 1.2)	0.006
Percentage drop in hemoglobin	17.3 (10.1, 21.7)	7.2 (3.5, 13.4)	<0.001
Re-imaging after biopsy	12 (80%)	19 (13%)	<0.001
Time to reimaging	28.6 (3.8, 74.0)	26.1 (18.7, 72.7)	0.60
Medium or large Hematoma	11 (79%)	0 (0%)	<0.001

Angiographic intervention after biopsy	3 (20%)	0 (0%)	<0.001
Death	1 (7%)	3 (2%)	0.28
Primary histological diagnosis			0.08
AIN	0 (0%)	24 (17%)	
ATN	4 (27%)	26 (18%)	
Diabetes	1 (7%)	27 (19%)	
Glomerular disease	6 (40%)	31 (22%)	
Arterionephrosclerosis	0 (0%)	17 (12%)	
Other	4 (27%)	18 (13%)	

*Complication is defined as presence of either biopsy-related transfusion, angiographic intervention to stop bleeding, or medium- to large-sized hematoma. CT, computerized tomography; BUN, blood urea nitrogen; IFTA, interstitial fibrosis and tubular atrophy. *Wilcoxon ranksum test, X^2, or Fishers exact test.*

Supplementary Table 4. Biopsy needle gauge, complications and risk factors in hospitalized patients with acute kidney disease

Characteristic	16G	18G	P
N	**88**	**71**	
Complications			
Any complication	12 (14%)	3 (4%)	0.06
Transfusions	10 (11%)	2 (3%)	0.07
Intervention	3 (3%)	0 (0%)	0.20
Hematoma	9 (11%)	2 (3%)	0.10
Death	3 (3%)	1 (1%)	0.68
Re-imaging	21 (24%)	10 (14%)	0.12
Drop in hemoglobin	0.8 (0.5, 1.6)	0.7 (0.3, 1.2)	0.07
Number of hemoglobin tests	12 (9, 17)	6 (3, 8)	<0.001
Risk factors			
Age	56 (43, 66)	60 (52, 70)	0.02
Female	36 (41%)	32 (45%)	0.03
Diabetes	26 (30%)	37 (53%)	0.012
Hypertension	50 (57%)	56 (79%)	0.03
Cirrhosis	11 (13%)	9 (13%)	0.05
CKD	42 (52%)	49 (74%)	0.002
BMI	28 (25, 32)	30 (25, 35)	0.08
AKI Stage1	42 (48%)	38 (56%)	0.26
AKI Stage2	26 (30%)	16 (24%)	0.13
Dialysis	7 (8%)	9 (13%)	0.43
Creatinine	4.2 (3.1, 6.5)	4.8 (3.3, 7.3)	0.22
BUN	51 (34, 76)	56 (38, 77)	0.40
BUN>60	34.0 (0.4, .)	31.0 (0.4, .)	0.23
Hemoglobin	9.4 (8.2, 10.5)	9.0 (7.9, 10.0)	0.93
Platelet	195 (144, 262)	213 (133, 302)	0.04
ICU	11 (13%)	5 (7%)	0.16
Passes	3 (2, 3)	3 (2, 3)	0.001
Fellow (vs. Attending)	66 (75%)	37 (52%)	<0.001
Nephrology (vs. Radiology)	86 (98%)	18 (25%)	<0.001
Desmopressin	74 (84%)	53 (75%)	0.10
Transfusion before biopsy	17 (19%)	14 (20%)	0.55
Adequacy			
Glomeruli obtained	11 (7, 15)	11 (5, 17)	0.63
Over 25 glomeruli obtained	5 (6%)	8 (11%)	0.25
Over 10 glomeruli obtained	51 (57%)	36 (52%)	0.52
Inadequate sample for diagnosis	1 (1%)	1 (1%)	0.70

*CT, computerized tomography; BUN, blood urea nitrogen; IFTA, interstitial fibrosis and tubular atrophy. *Wilcoxon ranksum test, X^2, or Fishers exact test.*

Supplementary Table 5. Association of needle gauge and department of proceduralist with transfusions in hospitalized patients with acute kidney disease

Risk factor	Model1	Model2	Model3
Needle gauge 16 vs. 18	4.4 (0.9, 20.9)	**5.9 (1.0, 32.8)**	4.5 (0.7, 27.5)
Nephrology vs. Radiology	6.5 (0.8, 51.4)	**10.6 (1.1, 103.0)**	9.2 (0.7, 120.8)

Odds ratio (95% CI); Model 1 is univariable association of risk factor with outcome of transfusion; Model 2 controls for platelet count, sex, and blood urea nitrogen level; Model 3 controls for training status of proceduralist along with all the variables of model 2

Supplementary Table 6. Comparison of kidney biopsies in the Yale and NIS cohorts

	Yale (159)	**NIS (53,315)**	**P-value**
Years	2015-2017	2012-2014	
Total biopsies	159	53,315	
Any blood transfusions during hospitalization	52 (33%)	15,930 (30%)	0.46
PRBC before	30 (19%)	n/a	n/a
PRBC after	34 (21%)	n/a	n/a
PRBC due to biopsy	12 (8%)	n/a	n/a
IR intervention after biopsy to stop bleeding	3 (2%)	925 (2%)	0.88
Hematoma	11 (8%)	2,850 (5%)	0.31
Death during hospitalization	4 (3%)	1,005 (2%)	0.74
Death related to biopsy complication	0	n/a	n/a

The nationwide inpatient sample does not have information on relationship of transfusion and death to kidney biopsy procedure.

Supplementary Table 7. Baseline characteristics in participants of the Yale biopsy cohort

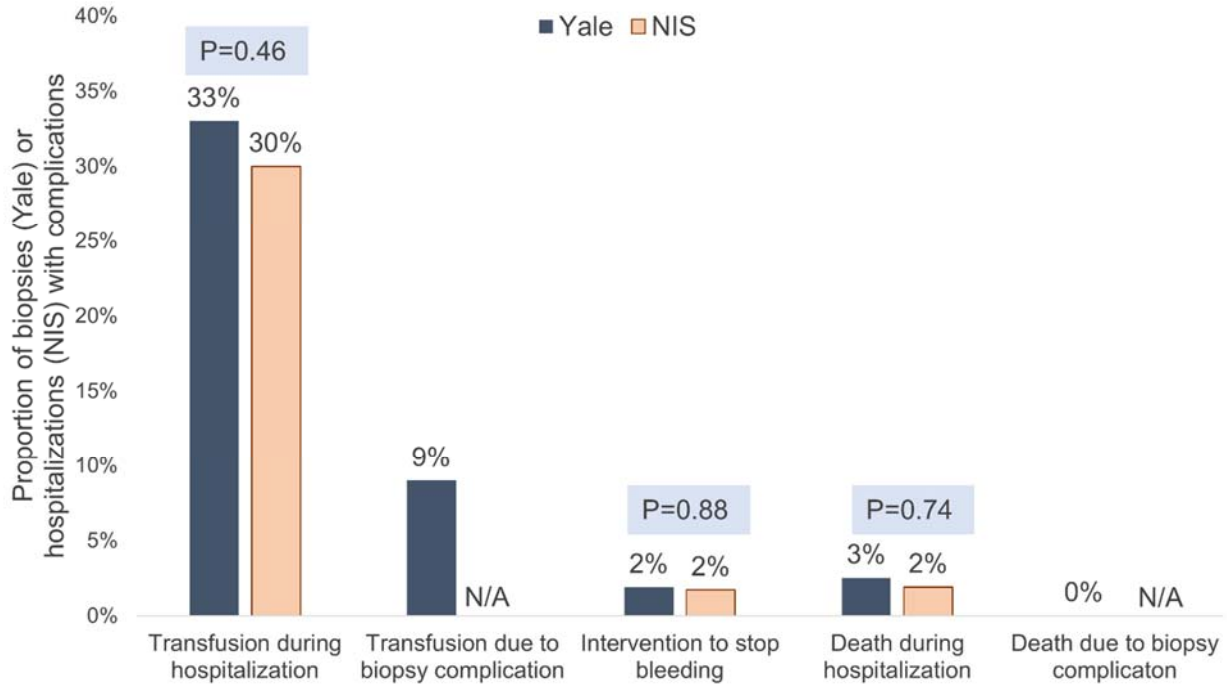
Characteristic	Hospitalized	Non-hospitalized	P-value*
N	159	97	
Demographics			
Age, years	59 (47, 68)	58 (49, 67)	0.78
Female	68 (43%)	53 (55%)	0.07
Black race	37 (23%)	33 (34%)	0.06
Diabetes	63 (40%)	32 (33%)	0.25
Hypertension	106 (67%)	85 (88%)	<0.001
Cirrhosis	20 (13%)	3 (3%)	0.009
Chronic kidney disease	91 (62%)	88 (91%)	<0.001
Body mass index (BMI), kg/m2	28 (25, 33)	29 (24, 35)	0.92
BMI>35kg/m2	32 (20%)	23 (24%)	0.47
Baseline Laboratory Features			.
Baseline Creatinine, mg/dl	1.3 (0.9, 1.9)	1.8 (1.4, 2.5)	<0.001
Baseline GFR, ml/min	46 (30, 74)	34 (22, 45)	<0.001
Baseline Protein to creatinine ratio, mg/mg	2.0 (0.6, 5.1)	1.5 (0.4, 3.7)	0.09
Dipstick protein ≥3+	111 (73%)	67 (74%)	0.86
Features at Biopsy			.
Acute kidney injury (AKI)	132 (83%)	7 (7%)	<0.001
Stage 1	80 (51%)	8 (9%)	
Stage 2 or higher	42 (27%)	0 (%)	
Dialysis	16 (10%)	0 (%)	
Acute kidney disease (excluding AKI)	27 (17%)	90 (93%)	
Creatinine, mg/dl	4.4 (3.2, 6.8)	2.3 (1.8, 3.6)	<0.001
Blood Urea Nitrogen, mg/dl	52 (35, 76)	34 (27, 49)	<0.001
BUN>60 mg/dl	65 (41%)	13 (13%)	<0.001
Hemoglobin, g/dl	9.2 (8.0, 10.2)	11.4 (10.5, 13.0)	<0.001
Hemoglobin<10 g/dl	116 (73%)	15 (15%)	<0.001
Platelets per mm^3	202 (142, 278)	245 (199, 280)	0.001
York Street campus (vs. St. Raphael campus)	128 (81%)	78 (80%)	0.99
Procedural Factors			.
Passes	3 (2, 3)	2 (3, 3)	0.66
Fellow (vs. Attending)	99 (64%)	27 (29%)	<0.001
Nephrology (vs. Radiology)	103 (65%)	55 (57%)	0.18
Needle Gauge 16 (vs. 18)	88 (55%)	49 (51%)	0.45
Ultrasound-guided (vs. CT)	118 (74%)	56 (58%)	0.008
Primary Histological diagnosis			0.007
AIN	24 (15%)	14 (14%)	
ATN	30 (19%)	8 (8%)	
Diabetes	28 (18%)	12 (12%)	
Glomerular disease	37 (23%)	19 (20%)	
Arterionephrosclerosis	17 (11%)	26 (27%)	
Other	23 (14%)	18 (19%)	

*CT, computerized tomography; BUN, blood urea nitrogen; IFTA, interstitial fibrosis and tubular atrophy. *Wilcoxon ranksum test, X^2, or Fishers exact test.*

Supplementary Table 8. Complications after kidney biopsy in non-hospitalized patients with acute kidney disease

Complication	All	Hospitalized	Non-hospitalized	P-value
N	**256**	**159**	**97**	
Blood transfusion for biopsy-related bleeding^	12 [5%]	12 [9%]	0 [0%]	0.003
Angiographic intervention to stop bleeding	3 [1%]	3 [2%]	0 [0%]	0.17
Death in 30 days*	4 [2%]	4 [3%]	0 [0%]	0.12
Hematoma	16 [7%]	11 [8%]	5 [5%]	0.52
Re-imaging after biopsy to check for bleeding	40 [16%]	31 [19%]	9 [9%]	0.03
Drop in hemoglobin, g/dl	0.8 (0.4, 1.3)	0.8 (0.4, 1.3)	0.9 (0.2, 1.4)	0.69
Hemoglobin drop >1 g/dl	74 [40%]	60 [39%]	14 [45%]	0.50
Hemoglobin drop >2 g/dl	19 [10%]	15 [10%]	4 [13%]	0.59
Number of hemoglobin tests after biopsy	5 (2, 8)	6 (3, 9)	1 (1, 2)	<0.001

Supplementary Figure 1. Comparison of nationwide trends with Yale complication data after kidney biopsy in hospitalized patients



Data on relationship of transfusion and death to kidney biopsy is not available (N/A) from the nationwide inpatient sample (NIS).

Supplementary Figure 2. STARD Flow diagram of non-hospitalized patients with acute kidney disease in the Yale Biopsy Cohort