Table S1. "*Repbase reduced list*".

Reference sequence	Reference length	Contig mapped	Average Coverage*	Repeat classes
L1 L1 Homo	5403	32	2.327041	L1 (Other)
L1HS L1 Homo	6064	13	0.730706	L1HS
L1PREC1 L1 Homo	6460	13	0.734056	L1P
ALR SAT Homo	171	10	9.877193	Alpha satellite
L1PA3 L1 Homo	902	10	3.370288	L1P
L1PA7 L1 Homo	901	10	4.039956	L1P
THE1_I LTR	1580	10	2.197468	ERV (Other)
ALR1 SAT Homo	171	7	6.760234	Alpha satellite
L1PA4 L1 Homo	902	7	1.949002	L1P
L1PA7_5 L1 Homo	1727	7	1.624783	L1P
AluY SINE1/7SL Primates	282	6	6	AluY
L1PA13 L1 Homo	910	5	2.102198	L1P
L1PA5 L1 Homo	901	5	1.400666	L1P
L1PA6 L1 Homo	901	5	1.866815	L1P
LTR12C ERV1 Homo	1577	5	1.257451	HERV-LTR
AluSx SINE1/7SL Primates	283	4	3.982332	AluS
L1PB2c L1 Homo	6582	4	0.231237	L1P
6kbHsap satellite Homo	6018	3	0.387172	Beta/acrocentric satellites
ALR_ SAT Primates	171	3	2.614035	Alpha satellite
AluSq SINE1/7SL Primates	284	3	3	AluS
L1PA8 L1 Homo	919	3	0.603917	L1P
L1PREC2 L1 Homo	8145	3	0.198772	L1P
LSU-rRNA_Hsa rRNA Metazoa	5035	3	0.726117	rRNA
HERVH ERV1 Eutheria	7713	2	0.190976	HERV
L1PB1 L1 Homo	898	2	0.888641	L1P
LTR7A ERV3 Homo	450	2	0.951111	HERV-LTR
MSTA ERV3 Primates	428	2	1.995327	ERV (Other)
SVA_D SINE Homo	1386	2	0.87518	SVA
THE1B ERV3 Hominidae	364	2	1.629121	ERV (Other)
THE1C ERV3 Homo	375	2	1.338667	ERV (Other)
THE1D ERV3 Homo	381	2	1.587927	ERV (Other)
ALR2 SAT Homo	179	1	0.960894	Alpha satellite
AluJb SINE1/7SL Primates	283	1	0.918728	AluJ
AluSp SINE1/7SL Primates	284	1	1	AluS
AluSq2 SINE1/7SL Primates	286	1	1	AluS
AluSz SINE1/7SL Primates	283	1	1	AluS
AluYa1 SINE1/7SL Primates	282	1	1	AluY
AluYb8 SINE1/7SL Homo	289	1	1	AluY
BSR SAT Homo	136	1	1	Beta/acrocentric satellites
HERV9 ERV1 Homo	8399	1	0.062746	HERV
HERVK11DI ERV2 Homo	7752	1	0.282895	HERV

HERVL ERV3 Homo	5654	1	0.074637	HERV
HSATI SAT Primates	577	1	0.989601	Human satellites
HSATII SAT Primates	170	1	0.905882	Human satellites
L1MA2 L1 Homo	1051	1	0.195052	L1 (Other)
L1MA9 L1 Homo	1059	1	0.167139	L1 (Other)
L1PA10 L1 Homo	915	1	0.215301	L1P
L1PA14 L1 Homo	908	1	0.431718	L1P
L1PA15 L1 Homo	912	1	0.319079	L1P
L1PA16 L1 Homo	913	1	0.508215	L1P
L1PA16_5 L1 Homo	4083	1	0.161891	L1P
L1PA2 L1 Homo	902	1	0.189579	L1P
LTR12 ERV1 Primates	826	1	0.478208	HERV-LTR
LTR12E ERV1 Homo	1322	1	0.217852	HERV-LTR
LTR5_Hs ERV2 Primates	968	1	0.713843	HERV-LTR
MER11C ERV2 Homo	1071	1	0.45098	ERV (Other)
MLT2A1 ERV3 Homo	444	1	0.585586	ERV (Other)
MLT2A2 ERV3 Homo	549	1	0.260474	ERV (Other)
SSU-rRNA_Hsa rRNA Metazoa	1869	1	1	rRNA
SVA_B SINE Homo	1383	1	0.229212	SVA
THE1A ERV3 Homo	355	1	0.833803	ERV (Other)

*Note. * Coverage referred to the mapping of the contig's consensus sequences versus the RepBase full list consensus sequence.*

Table S2. Count per million (CPM) of 100 bp sequences corresponding to different classes of repetitive DNA elements, in mono- and di-nucleosomal cfDNA fragments

Repetitive DNA family	**Mono-nucleosomal cfDNA (< 250 bp)**	**Di-nucleosomal cfDNA (> 250 bp)**	**P-value$^{(u)}$**	**P-value$^{(a)}$**
	(Mean +- sd)	**(Mean +- sd)**		
rRNA	1754 ± 410	4417 ± 3107	<0.001	<0.01
Alpha satellites	161729 ± 12483	129164 ± 13488	<0.001	<0.001
Beta/acrocentric satellites	17500 ± 1333	20688 ± 3260	<0.001	<0.001
Human satellites	38885 ± 6670	41298 ± 7920	<0.05	n.s.
SVA	5779 ± 533	6943 ± 1328	<0.001	<0.01
Alu-J	57247 ± 2289	65155 ± 5155	<0.001	<0.001
Alu-S	209359 ± 7866	243295 ± 23819	<0.001	<0.001
Alu-Y	55080 ± 2217	66110 ± 6394	<0.001	<0.001
HERV	21863 ± 894	22885 ± 2114	<0.05	n.s.
HERV-LTR	13360 ± 839	17344 ± 1824	<0.001	<0.001
Other ERV	78258 ± 2863	85281 ± 5732	<0.001	<0.001
L1HS	43495 ± 1536	40505 ± 5445	<0.05	n.s.
L1P	202173 ± 8364	175795 ± 9774	<0.001	<0.001
L1 (Other)	93095 ± 3793	82088 ± 7236	<0.001	<0.001

Note: $^{(u)}$ = Paired sample T test P-value, unadjusted; $^{(a)}$= Paired sample T test P-value, Bonferroni adjusted considering the multiple testing for 14 repeat classes

Table S3-A. Description of clinical and laboratory characteristics of the patients.

	Mean (s.d.)	**Min.-max.**	**Percentage**	**N° of cases**
Patients' characteristics				
Age, (yrs) mean (s.d.)	87.31 (4.63)	80.09-96.07		24
Survival, Time to event (months)	13.58 (10.73)	0-24		24
Survival, categorical				
1-24 months			(50%)	12
> 24 months			(50%)	12
Sex, n (%)				
Female			(41.7%)	10
Male			(58.3%)	14
Diagnosis at admission				
Hearth failure, n (%)			100%	24
*Comorbidities**				
Chronic kidney disease (CKD)			45.83%	11
Hypertension			87.5%	21
CAD/PAD			33.33 %	8
Cardiac arrhytmias			41.66 %	10
Diabetes/dyslipidemia			37.5 %	9
Anemia			33.33 %	8
Routine laboratory parameters				
	Mean (s.d.)	**Min.-max.**	**%**	**N° of cases**
WBC x10^3/µl	10.32 (5.30)	5.07-29.01		24
RBC x10^6/µl	3.90 (0.60)	2.96-4.94		24
Neutrophils x10^3/µl	8.25 (5.01)	3.20-25.82		24
NLR	8.58 (8.09)	1.81-31.81		24
Creatinine, (mg/dL)	1.42 (0.58)	0.70-2.90		24
eGFR, (ml/min)	46.08 (18.57)	13.00-80.00		24
Troponin, (pg/ml)	54.69 (43.37)	7.24-215.70		20
Nt-proBNP, (pg/ml)	7345.75 (7474.44)	247-26438		16
CRP, (mg/dl)	7.29 (7.33)	0.11-18.63		15
cfDNA parameters by Real-time PCR (Alu DNA quantification)				
	mean (s.d.)	**Min.-max.**	**%**	**N° of cases**
Alu 115 ng/ml	46.14 (48.07)	2.75-206.75		24
Alu 247 ng/ml	9.70 (8.47)	1.00-32.75		24
Alu 247/115	0.26 (0.14)	0.10-0.76		24

Alu 247/115 (categorical)				
(tertile 1) Low integrity			(45.8%)	11
(tertile 2) Intermediate integrity			(29.2%)	7
(tertile 3) High integrity			(25%)	6
Other cfDNA parameters *(Agilent Tape Station Screen Tape Analysis)*				
	mean (s.d.)	**Min.-max.**	**%**	**N° of cases**
Plasma concentration of mono-nucleosomal cfDNA by H.S. screen tape (range 100-280bp), pmol/L	593.60 (458.60)	60.40-1690.00		21
Plasma concentration of di-nucleosomal and tri-nucleosomal cfDNA by H.S. screen tape (range 280-700 bp), pmol/L	48.70 (31.57)	11.90-99.20		21
cfDNA_integrity by H.S. screen tape (pmol/L range 280-700bp)/ (pmol/L range 100-280bp)	0.11 (0.053)	0.04-0.21		21

*Note: * additional (less frequent) comorbidities: Chronic diseases of the digestive system, n=2; Acute diseases of the digestive system, n=4; Acute Diseases of the urinary system, n=2; Degenerative diseases of the CNS, n=4; Bone & Muscle Diseases, n=2; Endocrine, Nutritional and Metabolic Diseases, n=2; COPD, n=5; pneumonia, n= 1; Unspecified pleural Effusion, n=3; acute respiratory failure, n=5*

Table S3-B. Description of clinical and laboratory characteristics of the patients in the two subgroups with different outcome

	Survived after follow-up				**Not survived after follow-up**				
	Mean (s.d.)	Min.-max.	Percentage	N° of cases	Mean (s.d.)	Min.-max.	Percentage	N° of cases	p-value
Patients' characteristics									
Age, (yrs)	86.65 (5.59)	80.09-96.07		12	87.97 (3.56)	81.07-92.14		12	0.347§
Survival, Time to event (months)	24 (0.00)	24-24		12	3.17 (1.99)	0-6		12	
Sex, n (%)									
Female			(41.7%)	5			(41.7%)	5	1.00¥
Male			(58.3%)	7			(58.3%)	7	
Comorbidities									
Chronic kidney disease (CKD)									
Yes			58.3 %	7			50%	6	1.00¥

No			41.7 %	5			50%	6	
Hypertension									
Yes			0 %	0			25%	3	0.217¥
No			100 %	12			75%	9	
CAD/PAD									
Yes			58.3 %	7			75%	9	0.667¥
No			41.7 %	5			25%	3	
Cardiac arrhytmias									
Yes			75.0 %	9			41.7%	5	0.214¥
No			25.0 %	3			58.3%	7	
Diabetes/dyslipidemia									
Yes			50.0 %	6			75 %	9	0.400¥
No			50.0 %	6			25 %	3	
Anemia									
Yes			75.0 %	9			58.3 %	7	0.667¥
No			25.0 %	3			41.7 %	5	
Routine laboratory parameters									
WBC x10^3/µl	8.02	5.07-14.27		12	12.62	6.00-29.01		12	**0.008**
RBC x10^6/µl	3.75	2.96-4.35		12	4.05	3.21-4.94		12	0.219
Neutrophils x10^3/µl	6.04	3.20-11.74		12	10.44	4.98-25.82		12	0.713
NLR	5.71	1.81-15.21		12	11.45	2.61-31.81		12	0.143
Creatinine, (mg/dL)	1.54	0.90-2.90		12	1.30	0.70-2.40		12	0.410
eGFR, (ml/min)	42.75	13.00-78.00		12	49.41	18.00-80.00		12	0.514
Troponin, (pg/ml)	43.63	7.24-96.50		10	65.75	22.98-215.70		10	0.280
Nt-proBNP, (pg/ml)	9185.56	2435-26438		9	4980.29	247-12990		7	0.351
CRP, (mg/dl)	6.72	0.11-18.63		8	7.98	1.60-18.58		7	0.336

Note: § Mann-Whitney U test. ¥ Fisher exact test.

Table S4. Correlation (Spearman rho) between cfDNA parameters and parameters of clinical risk

	Age	**Time to event (days)**	**NLR (n=24)**	**Wbc**	**Rbc**	**Creatinine**	**eGFR (n=24)**	**Troponin (n=20)**	**Nt-proBNP (n= 16)**	**CRP (n=15)**
Dinucleosomal/mononucleosomal cfDNA ratio on H.S. Screen Tape, pg/ul (n=21)	0.179	-0.051	-0.121	-0.139	0.136	**0.523***	**-0.517***	0.252	0.126	0.473
Dinucleosomal/mononucleosomal cfDNA in NGS reads (n=24)	-0.043	0.192	-0.226	-0.086	0.209	0.234	-0.248	-0.163	-0.124	-0.168

*Note: * = p-value < 0.05.*

Table S5. cfDNA composition of repetitive DNA families in patients groups with different survival

		Mononucleosomal cfDNA			Dinucleosomal cfDNA		
Repeat class	**Survival (1 = deceased)**	**Mean [95% C.I.]**	**Median (IQR)**	**P-value[u]**	**Mean [95% C.I.]**	**Median (IQR)**	**P-value[u]**
Alu-J	0	$5.72x10^{04}$ ($5.59x10^{04}$ – $5.84x10^{04}$)	$5.69x10^{04}$ ($3.25x10^{03}$)	0.799	$6.37x10^{04}$ ($6.06x10^{04}$-$6.68x10^{04}$)	$6.28x10^{04}$ ($4.66x10^{03}$)	0.128
	1	$5.73x10^{04}$ ($5.56x10^{04}$-$5.90x10^{04}$)	$5.77x10^{04}$ ($4.42x10^{03}$)		$6.66x10^{04}$ ($6.33x10^{04}$-$6.99x10^{04}$)	$6.54x10^{04}$ ($5.27x10^{03}$)	
Alu-S	0	$2.09x10^{05}$ ($2.05x10^{05}$-$2.14x10^{05}$)	$2.10x10^{05}$ ($6.31x10^{03}$)	0.932	$2.37x10^{05}$ ($2.25x10^{05}$-$2.49x10^{05}$)	$2.38x10^{05}$ ($2.29x10^{04}$)	0.443
	1	$2.10x10^{05}$ ($2.04x10^{05}$-$2.15x10^{05}$)	$2.09x10^{05}$ ($1.27x10^{04}$)		$2.50x10^{05}$ ($2.33x10^{05}$-$2.67x10^{05}$)	$2.49x10^{05}$ ($2.82x10^{04}$)	
Alu-Y	0	$5.50x10^{04}$ ($5.34x10^{04}$-$5.65x10^{04}$)	$5.50x10^{04}$ ($3.17x10^{03}$)	0.843	$6.48x10^{04}$ ($6.12x10^{04}$-$6.85x10^{04}$)	$6.47x10^{04}$ ($7.57x10^{03}$)	0.443
	1	$5.52x10^{04}$ ($5.39x10^{04}$-$5.65x10^{04}$)	$5.50x10^{04}$ ($3.23x10^{03}$)		$6.74x10^{04}$ ($6.29x10^{04}$-$7.18x10^{04}$)	$6.69x10^{04}$ ($1.18x10^{04}$)	
Alu (total)	0	$3.21x10^{05}$ ($3.14x10^{05}$-$3.28x10^{05}$)	$3.23x10^{05}$ ($1.12x10^{04}$)	1.00	$3.65x10^{05}$ ($3.48x10^{05}$-$3.82x10^{05}$)	$3.61x10^{05}$ ($3.13x10^{04}$)	0.178
	1	$3.22x10^{05}$ ($3.14x10^{05}$-$3.30x10^{05}$)	$3.19x10^{05}$ ($1.83x10^{04}$)		$3.84x10^{05}$ ($3.63x10^{05}$-$4.05x10^{05}$)	$3.83x10^{05}$ ($3.95x10^{04}$)	
L1HS	0	$4.33x10^{04}$ ($4.22x10^{04}$-$4.44x10^{04}$)	$4.37x10^{04}$ ($3.23x10^{03}$)	0.551	$3.97x10^{04}$ ($3.77x10^{04}$-$4.17x10^{04}$)	$4.03x10^{04}$ ($4.47x10^{03}$)	0.378
	1	$4.37x10^{04}$ ($4.28x10^{04}$-$4.46x10^{04}$)	$4.37x10^{04}$ ($2.01x10^{03}$)		$4.13x10^{04}$ ($3.68x10^{04}$-$4.58x10^{04}$)	$4.13x10^{04}$ ($4.85x10^{03}$)	
ALR	0	$1.64x10^{05}$ ($1.56x10^{05}$-$1.72x10^{05}$)	$1.66x10^{05}$ ($1.79x10^{04}$)	0.630	$1.29x10^{05}$ ($1.22x10^{05}$-$1.37x10^{05}$)	$1.30x10^{05}$ ($1.09x10^{04}$)	0.799
	1	$1,60x10^{05}$ ($1,52x10^{05}$-$1,68x10^{05}$)	$1,60x10^{05}$ ($2,11x10^{04}$)		$1,29x10^{05}$ ($1,19x10^{05}$-$1,39x10^{05}$)	$1,34x10^{05}$ ($2,06x10^{04}$)	

Note: [u] = Mann-Whitney, P-value, unadjusted.

Table S6. Fold change of repeat families in cfDNA in patients groups with or without CKD

Repeat class	**CKD (1=ckd)**	**Mean (95% C.I.)**	**Median (IQR)**	**P-value[u]**	**P-value[a]**
FC_AluJ	0	1.14 (1.09-1.20)	1.13 (0.08)	0.865	n.s.
	1	1.13 (1.09-1.18)	1.13 (0.10)		
FC_AluS	0	1.20 (1.16-1.25)	1.20 (0.08)	**0.006**	**0.03**
	1	1.11 (1.07-1.16)	1.12 (0.08)		
FC_AluY	0	1.21 (1.14-1.29)	1.20 (0.19)	0.608	n.s.
	1	1.18 (1.11-1.26)	1.17 (0.15)		
FCTot_Alu	0	1.19 (1.15-1.23)	1.19 (0.13)	**0.047**	n.s.
	1	1.13 (1.08-1.17)	1.13 (0.09)		

Note: [u] = Mann-Whitney. P-value. unadjusted; [a]= Mann-Whitney. P-value. Bonferroni adjusted considering the multiple testing for 3 categories (AluJ, AluS, AluY)