Morbidity and mortality of sickle cell disease patients is unaffected by splenectomy: evidence from three decades of follow-up in a high-income setting

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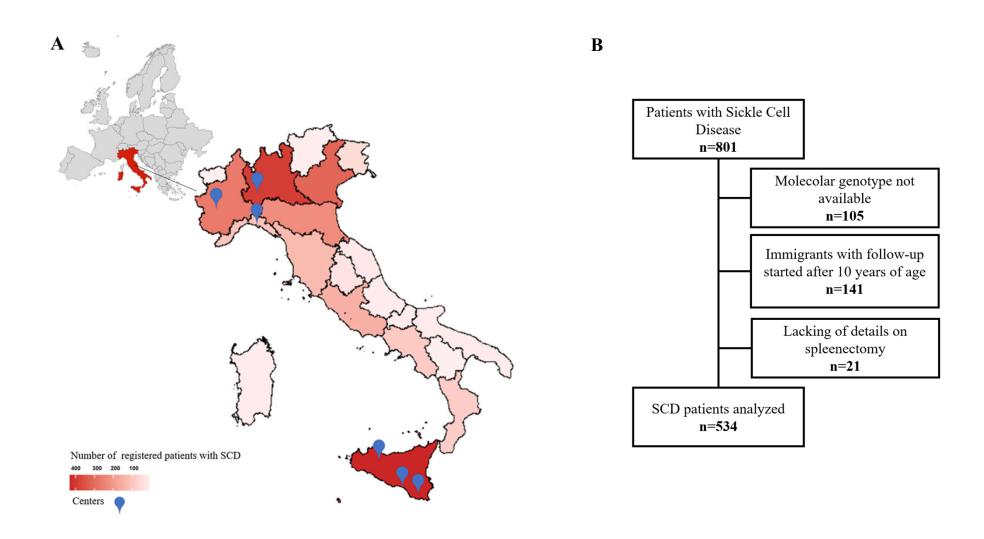


Figure S1. A. Distribution of sickle cell disease (SCD) in Italy and comprehensive centers for hemoglobinopathies with long-term followed-up patients with SCD patients (n=2,300). **B.** Flow-chart of study population (SCD: Sickle Cell Disease).

Study	Genotype	Country	Age	Splenectomies	Patients	Events per 100 observations	Prop. (%)	[95% CI]
Belhani et al (1984)	SS	Algeria	lower and greater than 15 yrs	0	42	<u> </u>	0.00	[0.00; 8.41]
Okoro (1989)	SS	Nigeria	children	4	4359	•	0.09	[0.03; 0.23]
Durosinmi et al (2005)	SS	Nigeria	16-48 (median, 21) years	3	71		4.23	[0.88; 11.86]
Diagne et al (2010)	SS	Senegal	mean age: 6.9 yrs	4	660		0.61	[0.17; 1.54]
Tolo-Diebkilé (2010)	SS	Ivory Coast	mean age 26.1 yrs	4	48	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	8.33	[2.32; 19.98]
Gale et al (2016)	SS	USA	0-21 yrs	9	112	- -	8.04	[3.74; 14.71]
Present study	SS	Italy	1-74 (median: 18)	18	187	- 	9.63	[5.81; 14.79]
Belhani et al (1984)	Sß	Algeria	lower and greater than 15 yrs	1	42	-	2.38	[0.06; 12.57]
Diagne et al (2010)	Sß	Senegal	mean age: 6.9 yrs	0	31	F	0.00	[0.00; 11.22]
Present study	Sß	Italy	1-78 (median: 41)	152	347		43.80	38.51; 49.20]
		•						
					5899	•	3.31	[2.88; 3.79]
						-	2.26	[0.58; 8.38]
						0 10 20 30 40 50 60		

Figure S2. Forest plot of observational studies reporting cases of surgical splenectomy in SCD for genotype SS (red) and S β , considered as S β $^{\circ}$ plus S β + (gray). The studies reported were included in the systematic review of Ladu et al. (2021).

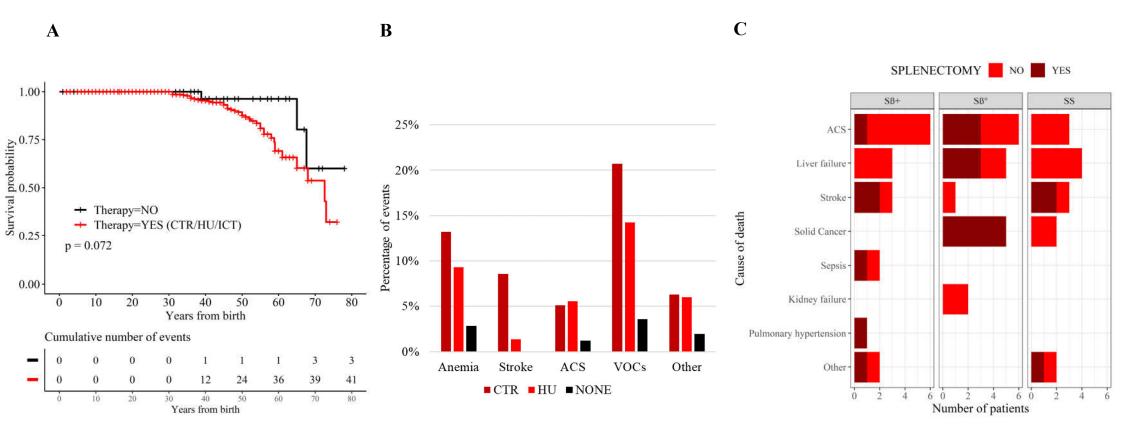


Figure S3. A. Survival probability for patients without therapy (NO) or treated with CTR, HU or ICT therapy. **B.** Percentage of sickle cell related events occurred in SCD patients by treatment type (HU/CTR/NONE). (CTR: chronic transfusion regimen; HU: hydroxyurea; ICT: iron chelation therapy). **C.** Causes of death in splenectomized (YES) or not-splenectomized (NO) patients with sickle cell disease according to genotypes