

2000 - 2010

Patients receiving anthracyclines:
N = 3081

Exclusion:

- No blood sample available, n=1588
- HER2 treatment, n=264
- Metastatic disease at baseline, previous oncological disease, n=236

Eligible for EMR review:
N = 993

2011 - 2018

Patients receiving anthracyclines:
N = 2028

Exclusion:

- No blood sample available, n=652
- HER2 treatment, n=399
- Metastatic disease at baseline, previous oncological disease, n=187

Eligible for EMR review:
N = 790

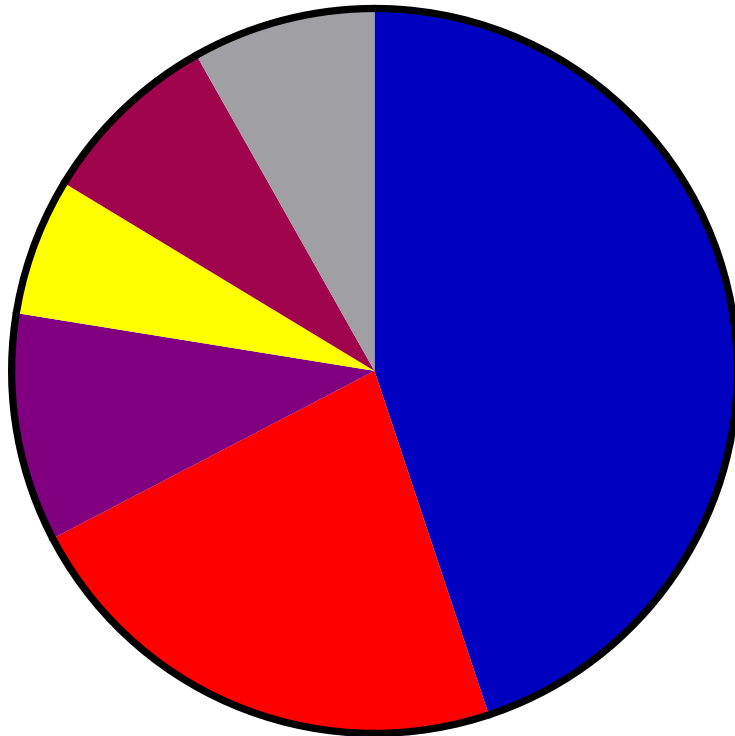
EMR reviewed:
N = 1783

Exclusion:

- No baseline or follow-up TTE, n=582
- Metastatic disease or second primary malignancy during follow-up, n=167
- Significant comorbidity, n=13
- HER2 treatment, n=17
- Preexisting cardiovascular disease, n=10
- Male, n=5

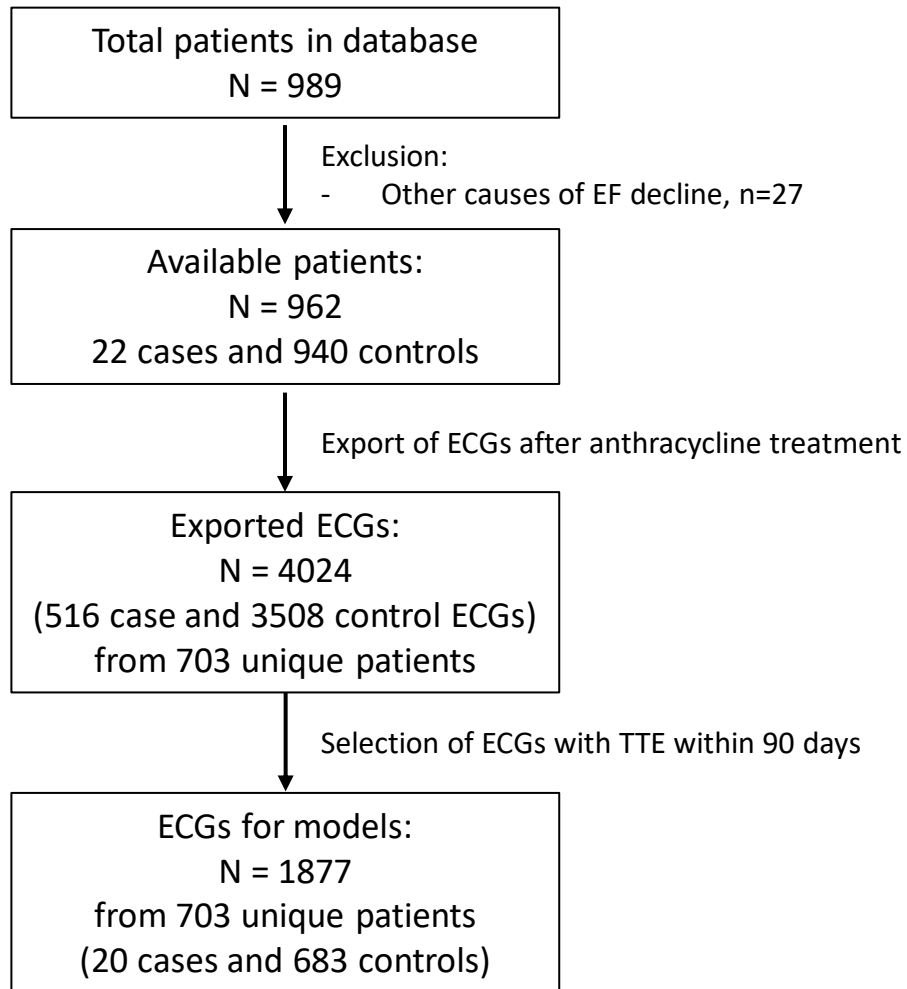
Eligible for current analysis:
N = 989

Causes of LV decline



- 45% Anthracycline-induced cardiomyopathy (n=22)
- 22% Ischemic heart disease (n=11)
- 10% Tachycardiomyopathy (n=5)
- 6% Valvular heart disease (n=3)
- 8% Other (n=4)
- 8% Unknown (n=4)

Total=49



- 313 ECGs from the 20 case patients
- 1564 ECGs from 683 control patients
- 156 ECGs mapped to TTEs that showed $EF \leq 35\%$
- 221 ECGs mapped to TTEs with $EF \leq 40\%$
- 261 ECGs mapped to TTEs with $EF \leq 45\%$
- 271 ECGs mapped to TTEs with $EF < 50\%$

Supplementary Table 1: Baseline characteristics total cohort

<u>Baseline characteristics</u>	<u>Total population</u> (n=989)	<u>Controls</u> (n=940)	<u>Cases</u> (n=22)	<u>p-value</u>
Age (at February 1st 2023, mean ± SD)	62.38 years (± 11.21)	62.04 years (± 11.22)	67.18 years (± 8.51)	0.02
Tumor characteristics				
- ER positivity	69.2% (n=681)	68.8% (n=647)	77.3% (n=17)	0.49
- PR positivity	60.1% (n=596)	60.4% (n=568)	59.1% (n=13)	>0.99
<i>Pathological stage</i> (data available n=748)				0.07
- IA/IB	11.9% (n=89)/4% (n=30)	11.9% (n=84)/4.1% (n=29)	21.4% (n=3)/0% (n=0)	
- IIA/IIB	28.9% (n=216)/30.1% (n=225)	29% (n=205)/30.2% (n=214)	14.3% (n=2)/28.6% (n=4)	
- IIIA/IIIB/IIIC	19% (n=142)/0.3% (n=2)/5.3% (n=40)	19.1% (n=135)/0.1% (n=1), 5.1% (n=36)	14.3% (n=2)/ 0% (n=0)/21.4% (n=3)	
- IV	0.4% (n=3)	0.4% (n=3)	0% (n=0)	
<i>grade</i>				0.42
- 1	3.9% (n=39)	3.8% (n=36)	4.5% (n=1)	

- 2	40.4% (n=400)	41% (n=385)	27.3% (n=6)	
- 3	54.9% (n=543)	54.7% (n=514)	68.2% (n=15)	
Setting				0.80
- Adjuvant	77.6% (n=767)	76.9% (n=723)	81.8% (n=18)	
- Neoadjuvant	22.4% (n=222)	23.1% (n=217)	18.2% (n=4)	
Oncological treatment				0.03
- FEC (5FU, Epirubicin, Cyclophosphamide)	69.3% (n=685)	68.2% (n=641)	90.9% (n=20)	
- EC (Epirubicin, Cyclophosphamide)	29.5% (n=292)	30.6% (n=288)	9% (n=2)	
- AC (Adriamycin, Cyclophosphamide)	1% (n=10)	1% (n=9)	0% (n=0)	
- CAF (Cyclophosphamide, Adriamycin, 5FU)	0.2% (n=2)	0.2% (n=2)	0% (n=0)	
Number of cycles with anthracyclines received	3.86 (± 1.16)	3.82 (± 1.12)	5.05 (± 1.43)	<0.01
Radiotherapy	94.5% (n=935)	95% (n=888)	95.5% (n=21)	>0.99
Cardiovascular risk factors				
- smoking (data available n=885)	39.2% (n=348)	38.9% (n=326)	47.7% (n=10)	0.50
- hypertension (data available n=988)	24.6% (n=243)	24.2% (n=227)	13.6% (n=3)	0.32
- diabetes (data available n=989)	4.6% (n=45)	4.1% (n=39)	9% (n=2)	0.24

- obesity (data available n=985)	22% (n=218)	21.8% (n=204)	22.7% (n=5)	>0.99
- hypercholesterolemia (data available n=986)	25.6% (n=252)	24.7% (n=231)	27.2% (n=6)	0.80
- family history of cardiovascular disease (data available n=368)	32.1% (n=118)	32.9% (n=107)	12.5% (n=2)	0.10
baseline EF (± SD)	63 ± 6%	63 ± 6%	63 ± 6%	>0.99