Gasto cardíaco por ECOTT vs Fick

Parte 3: Análisis Índice Cardíaco

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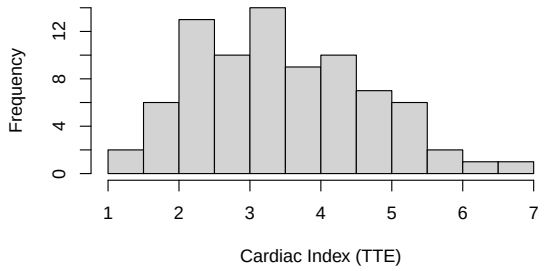
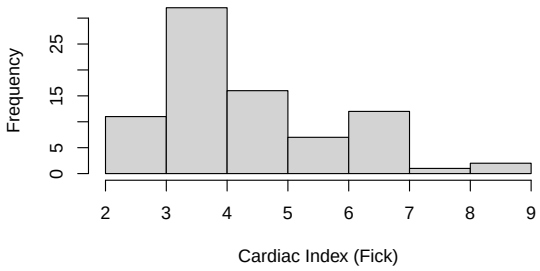
Cardiac Index

The distribution of cardiac index values for both methods is skewed as shown bellow.



(a) TTE

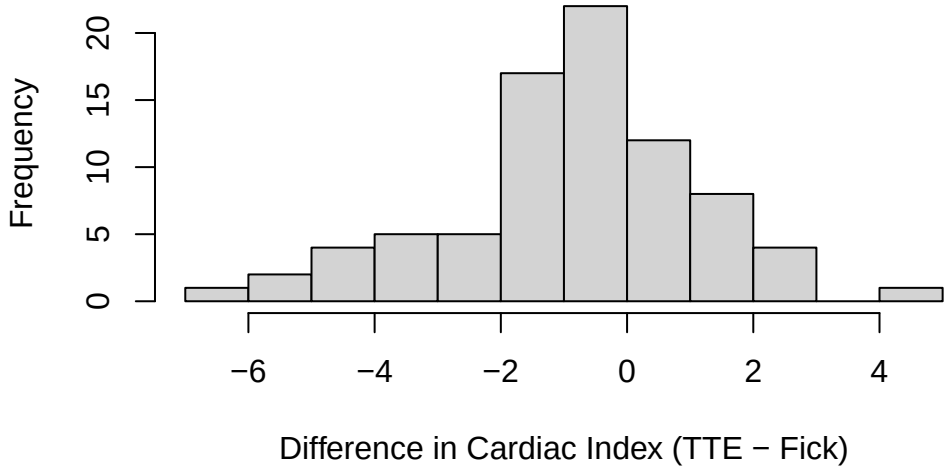


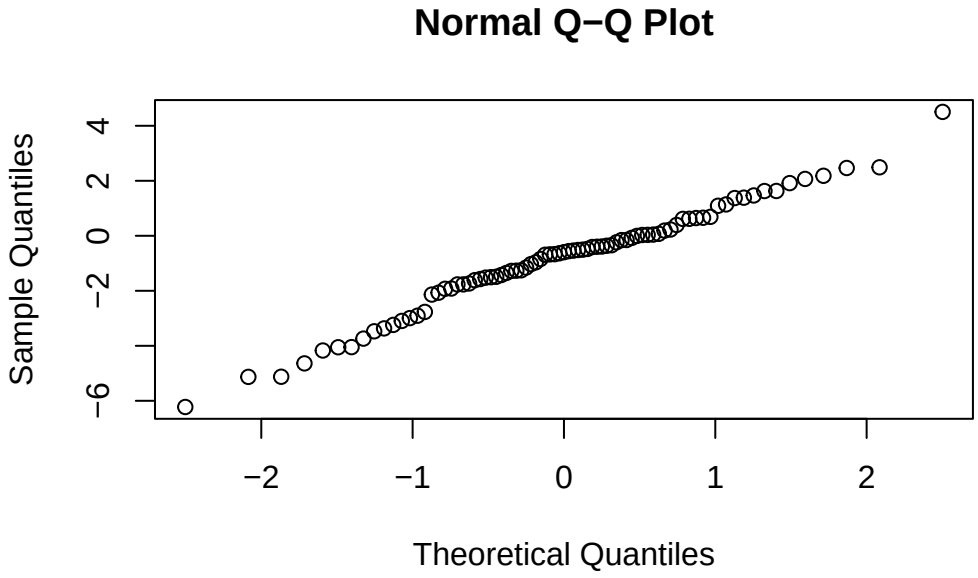
(a) Fick

Thus, bootstrapping is used to calculate the mean with 95% CI:

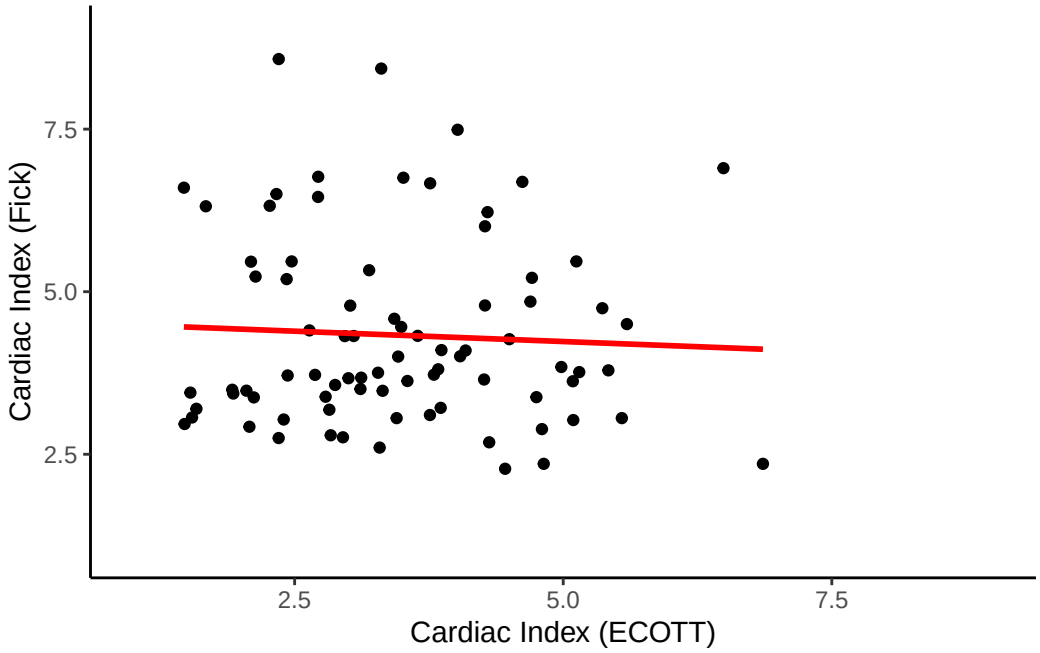
The mean cardiac index for TTE is 3.47 L/min/m² (95% CI: 3.21 to 3.74), and for Fick, 4.33 L/min/m² (95% CI: 4.04 to 4.67).

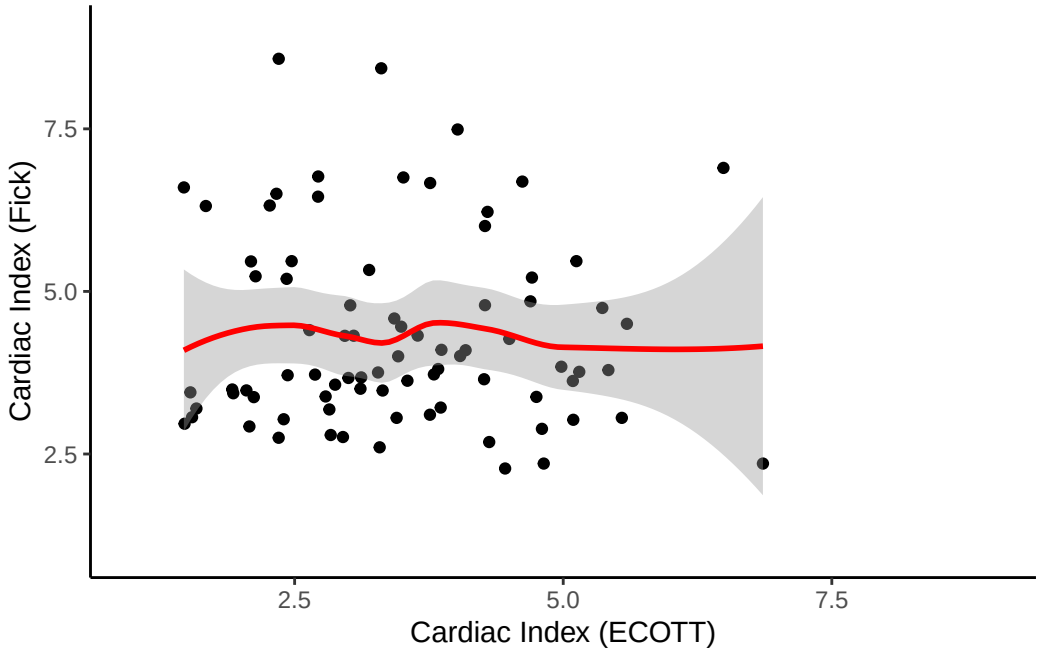
However, the distribution of differences between the two methods is approximately normal.





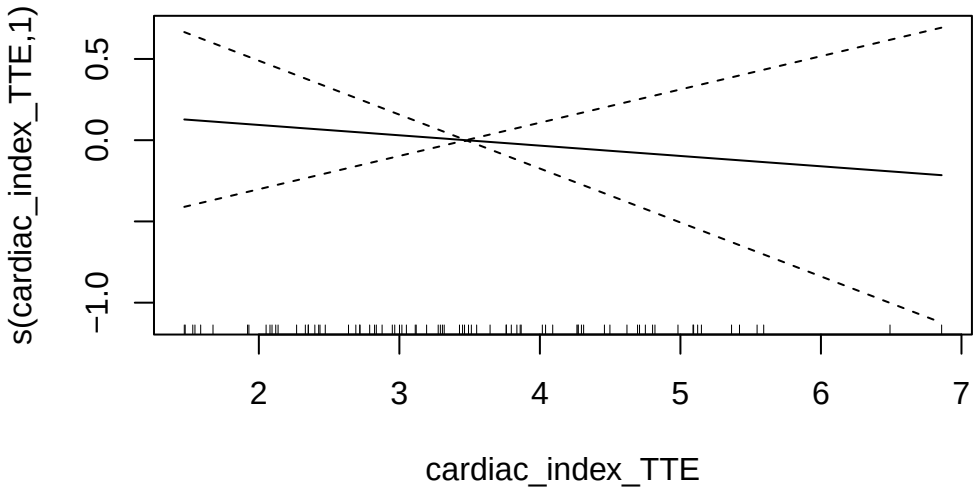
Assuming a linear and non-linear relationship





Examine if non-linear term is significantly better than linear term

```
Family: gaussian
Link function: identity

Formula:
cardiac_index_Fick ~ s(cardiac_index_TTE)

Parametric coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)   4.3307     0.1621   26.72   <2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Approximate significance of smooth terms:
                     edf Ref.df     F p-value
s(cardiac_index_TTE)   1      1 0.225   0.637

R-sq.(adj) =  -0.00978   Deviance explained = 0.284%
GCV = 2.1819  Scale est. = 2.128     n = 81
```



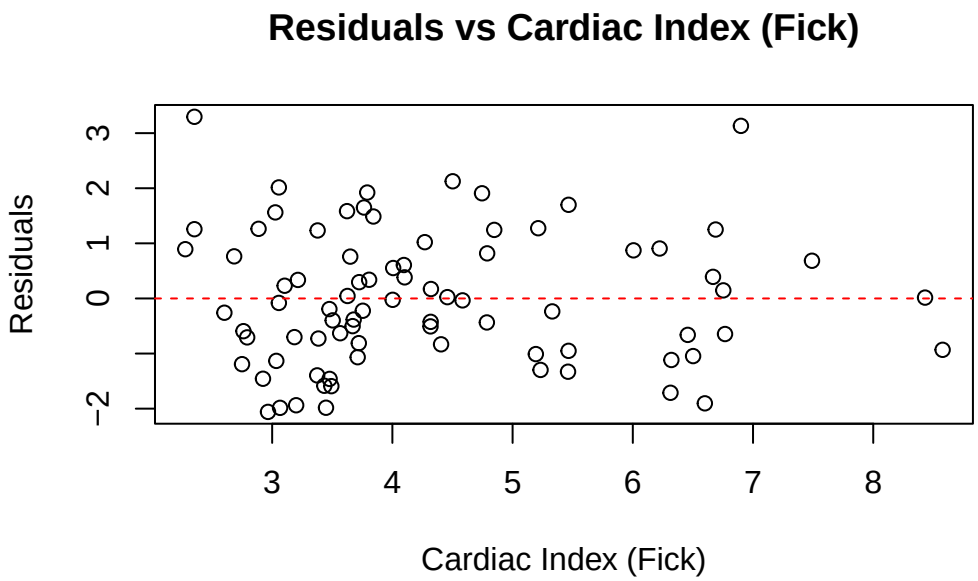
Non-linear relationship is not significantly better than linear relationship. Thus, I will model as linear relationship.

Pearson correlation

```
    Pearson's product-moment correlation

data:  data$cardiac_index_TTE and data$cardiac_index_Fick
t = -0.47421, df = 79, p-value = 0.6367
alternative hypothesis: true correlation is not equal to 0
95 percent confidence interval:
 -0.2685034  0.1670148
sample estimates:
        cor
-0.05327754
```

Linear regression

```
Call:
lm(formula = cardiac_index_TTE ~ cardiac_index_Fick, data = data)

Residuals:
    Min      1Q  Median      3Q     Max
-2.0591 -0.9323 -0.0813  0.8727  3.2967

Coefficients:
                   Estimate Std. Error t value Pr(>|t|)
(Intercept)         3.66720    0.42949   8.539 7.75e-13 ***
cardiac_index_Fick -0.04462    0.09409  -0.474    0.637
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 1.222 on 79 degrees of freedom
Multiple R-squared:  0.002838,  Adjusted R-squared:  -0.009784
F-statistic: 0.2249 on 1 and 79 DF,  p-value: 0.6367
```



Linear Mixed Effects Model

```
Linear mixed model fit by REML ['lmerMod']
Formula: cardiac_index_Fick ~ cardiac_index_TTE + (1 | ID) + (1 | time_point)
   Data: data

REML criterion at convergence: 269.2

Scaled residuals:
    Min      1Q  Median      3Q     Max
-1.6281 -0.3603 -0.1032  0.2624  2.4707

Random effects:
 Groups     Name        Variance Std.Dev.
 ID         (Intercept) 1.4125   1.1885
 time_point (Intercept) 1.4002   1.1833
 Residual               0.4453   0.6673
Number of obs: 81, groups:  ID, 52; time_point, 9

Fixed effects:
                  Estimate Std. Error t value
(Intercept)        5.10906    0.66721   7.657
cardiac_index_TTE -0.02765    0.11350  -0.244

Correlation of Fixed Effects:
            (Intr)
crdc_nd_TTE -0.649
```

Intraclass correlation coefficient (ICC)

```
Average Score Intraclass Correlation

  Model: twoway
  Type : agreement

  Subjects = 81
    Raters = 2
  ICC(A,2) = -0.0921

F-Test, H0: r0 = 0 ; H1: r0 > 0
F(80,65.7) = 0.9 , p = 0.675

95%-Confidence Interval for ICC Population Values:
 -0.588 < ICC < 0.265
```

Coefficient of variation (CV) and coefficient of error (CE)

The following calculation is the coefficient of variation (CV) for the overall averaged measurements, expressed as percentage:

Fick CV: 33.52%

TTE CV: 35%

Because there are multiple measurements that are averaged to produce the mean Cardiac Index for TTE, we can calculate the coefficient of error (CE) as suggested by Cecconi, et al.[1] The following calculations reproduce the structure of the table in their review article:

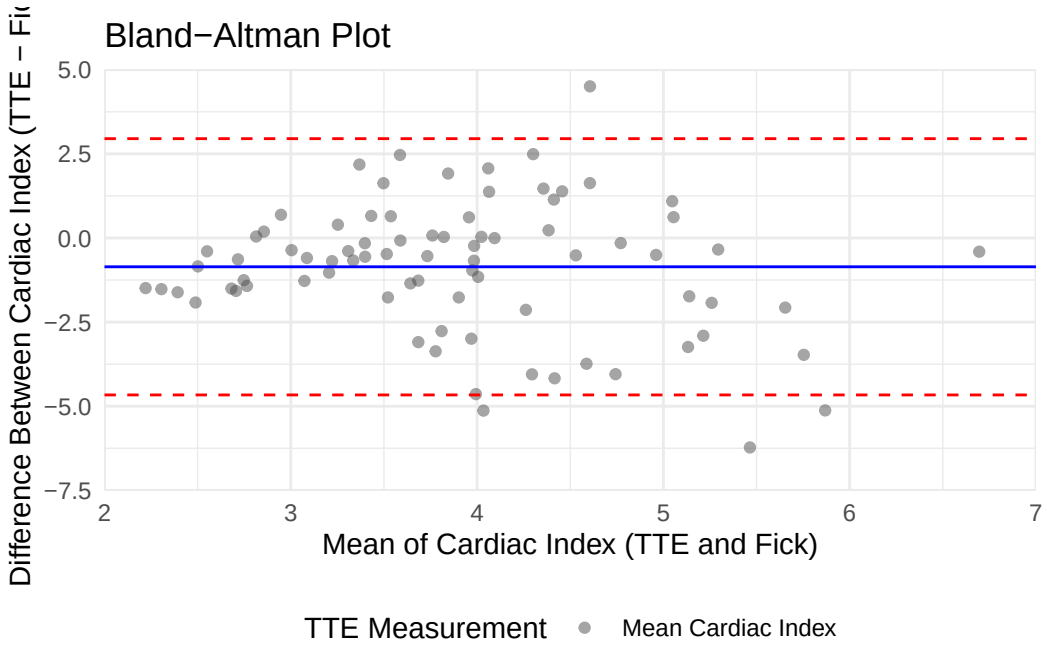
ID	CI 1 (TTE), L/min/m²	CI 2 (TTE), L/min/m²	CI 3 (TTE), L/min/m²	Mean CI TTE, L/min/m²	CV (%)	CE (%)	CI (Fick method), L/min/m²
1	3.18	3.59	3.10	3.29	8.02	4.63	2.60
2	7.31	6.51	6.76	6.86	5.96	3.44	2.35
2	4.93	4.90	4.62	4.82	3.52	2.03	2.35
3	2.30	2.42	2.34	2.35	2.74	1.58	8.58
3	2.67	2.77	2.72	2.72	1.83	1.05	6.46
4	1.54	1.61	1.49	1.55	3.74	2.16	3.07

CE: Coefficient of Error; CV: Coefficient of Variation; TTE: Transthoracic Echocardiography.

The mean CV of TTE for the repeated measurements per patient was 7.3% (95% CI: 6.2 to 8.7) and the CE was 4.2% (95% CI: 3.6 to 5), corresponding to a precision of 8.4% (95% CI: 7.2 to 10.1).

Bland-Altman Plot

Bland Altman-single measure

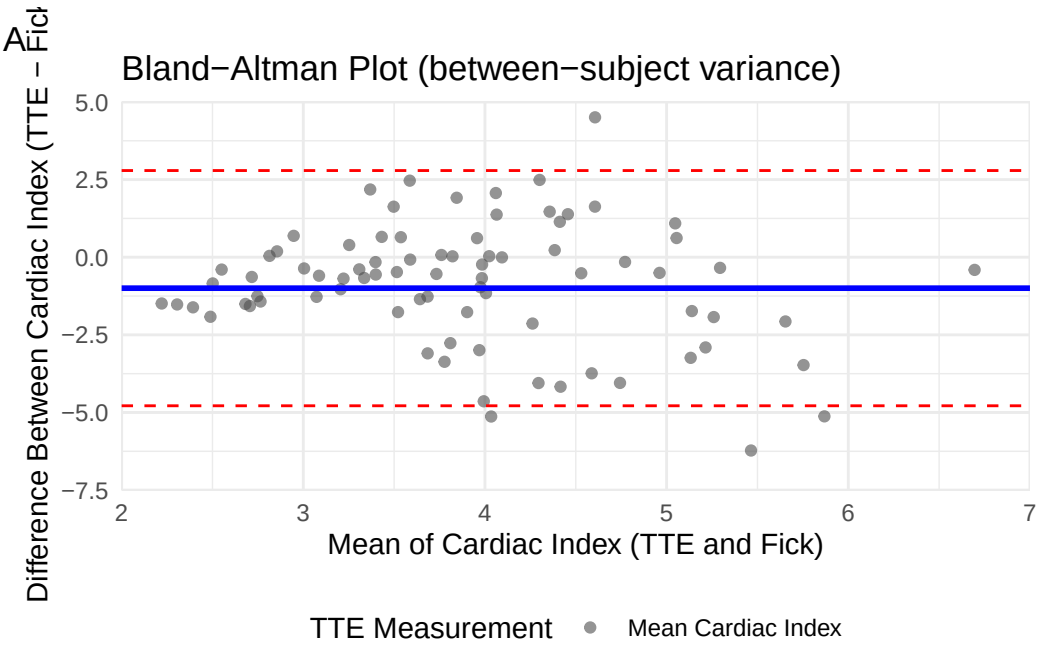


Systematic bias (Paired t-test)

```
    Paired t-test

data:  data$cardiac_index_TTE and data$cardiac_index_Fick
t = -3.9695, df = 80, p-value = 0.0001563
alternative hypothesis: true mean difference is not equal to 0
95 percent confidence interval:
 -1.2863075 -0.4272454
sample estimates:
mean difference
     -0.8567765
```

Bland Altman-repeated measures (random effects for between-subject variance)

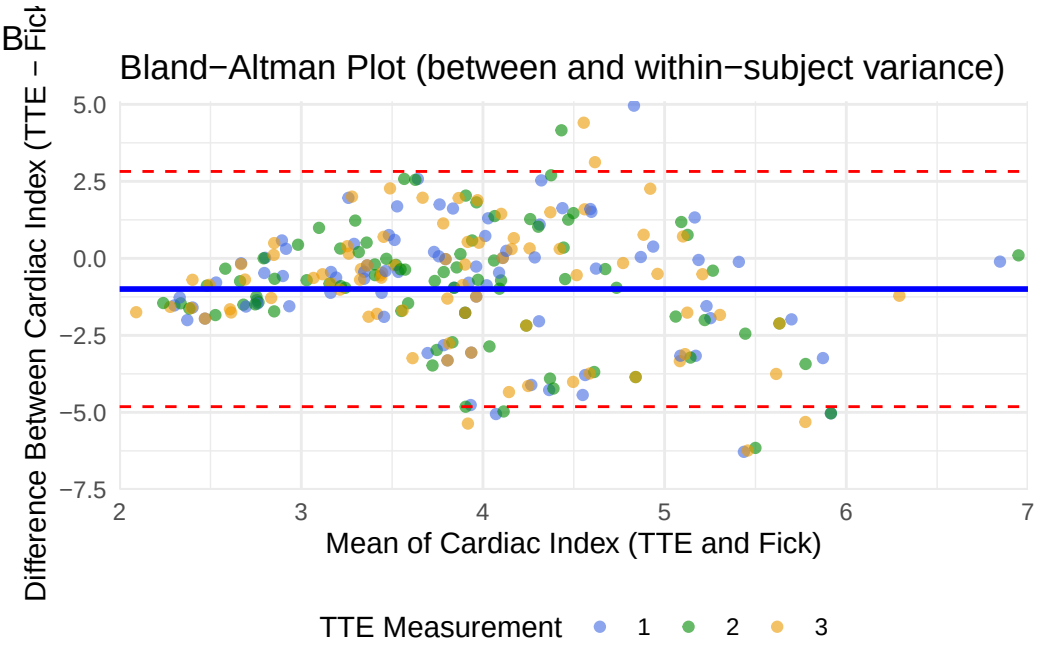
```
Linear mixed model fit by REML ['lmerMod']
Formula: differences ~ 1 + (1 | ID)
   Data: data

REML criterion at convergence: 319.4

Scaled residuals:
     Min       1Q   Median       3Q      Max
-2.22339 -0.30675 -0.05103  0.31807  2.02571

Random effects:
 Groups   Name        Variance Std.Dev.
 ID       (Intercept) 2.301    1.517
 Residual             1.433    1.197
Number of obs: 81, groups:  ID, 52

Fixed effects:
            Estimate Std. Error t value
(Intercept)  -0.9965     0.2570  -3.877
```



Bland Altman-repeated measures (random effects for between-subject variance and within-subject variance)

```
Linear mixed model fit by REML ['lmerMod']
Formula:
differences ~ 1 + (1 | ID) + (1 | ID:time_point) + (1 | TTE_measurement)
   Data: data_long

REML criterion at convergence: 476.3

Scaled residuals:
    Min      1Q  Median      3Q     Max
-2.6307 -0.4333 -0.0181  0.3925  2.4684

Random effects:
 Groups          Name        Variance Std.Dev.
 ID:time_point   (Intercept) 1.40369  1.1848
 ID              (Intercept) 2.30131  1.5170
 TTE_measurement (Intercept) 0.00000  0.0000
 Residual                    0.08906  0.2984
Number of obs: 243, groups:  ID:time_point, 81; ID, 52; TTE_measurement, 3

Fixed effects:
            Estimate Std. Error t value
(Intercept)  -0.9965     0.2570  -3.877
optimizer (nloptwrap) convergence code: 0 (OK)
boundary (singular) fit: see help('isSingular')
```

There was singularity in the prior model including a random effect for within-subject TTE measurements. Because this term is conceptually important to take into account the nested structure of the data, we will keep it in the model. Other alternatives would be to include it as a fixed effect, but this would not necessarily represent a meaningful variable to model.


Bland−Altman Plot (between and within−subject variance)
Difference Between Cardiac Index (TTE − Fick
5.0
2.5
0.0
−2.5
−5.0
−7.5
2
3
4
5
6
7
Mean of Cardiac Index (TTE and Fick)
TTE Measurement
1
2
3

Mean absolute difference (MAD)

The MAD for Cardiac Index is 1.6 (95% CI: 1.2 to 2).

Mean absolute percentage error (MAPE) and precision of Fick method

```
Precisionb (point estimate): 56.84 %

Precisionb (95% CI): 44.34 - 74.22 %
```

Summary

The mean cardiac index with the TTE method was 3.47 L/min/m² (95% CI: 3.21 to 3.74) and 4.33 L/min/m² (95% CI: 4.04 to 4.67) with the Fick method. The correlation between the two methods was rho = -0.05 (95% CI: -0.27 to 0.17, p=0.637). In a linear mixed model with random patient slopes, there was a change in Fick CI of -0.03 (95% CI: -0.26 to 0.2) L/min/m² for each unit change in mean TTE CI. The ICC between TCE and Fick CI -0.09 (95% CI: -0.59 to 0.26).

The mean absolute difference in CI between TTE and Fick was 1.59 (95% CI: 1.2 to 2) L/min/m². The coefficient of variation for an individual measurement of TTE was 35% and 33.52% for Fick. The mean CV of TTE for the repeated measurements per patient was 7.3% (95% CI: 6.2 to 8.7) and the CE was 4.2% (95% CI: 3.6 to 5), corresponding to a precision of 8.4% (95% CI: 7.2 to 10.1). The MAPE of the Fick method compared to TTE was 57.5% (95% CI: 45.5 - 74.6). The precision of the Fick method was 56.84% (95% CI: 44.34 to 74.22). The LSC was 11.9% (95% CI: 10.1 to 14.3) for TTE and 80.4% (95% CI: 62.7 to 105) for the Fick method.

Figure 2 shows the Bland-Altman plot for the repeated measures model with random effects for between-subject variance (Figure2A) and within-subject variance (Figure2B). The mean difference (systematic bias) between TTE and Fick CI was -1 (95% CI: -1.5 to -0.49, p = 0) L/min/m², with 95% limits of agreement of -4.81 to 2.82 L/min/m².

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