

Prevalence of cortisol cosecretion in patients with primary aldosteronism: role of metanephrine in adrenal vein sampling

Fabrizio Buffolo¹, Jacopo Pieroni^{1*}, Federico Ponzetto^{2*}, Vittorio Forestiero¹, Denis Rossato³, Paolo Fonio³, Antonello Nonnato², Fabio Settanni², Paolo Mulatero¹, Giulio Mengozzi^{2**}, Silvia Monticone^{1**}.

¹Division of Internal Medicine and Hypertension Unit, Department of Medical Sciences, University of Torino, 10126, Torino, Italy.

²Department of Laboratory Medicine, University of Torino, 10126 Torino, Italy

³Division of Radiology, University of Torino, 10126 Torino, Italy

* These authors contributed equally to this work and should be considered as joint second authors.

** These authors contributed equally to this work and should be considered as joint last authors.

Summary

Tables

Table S1. Clinical and biochemical characteristics of patients with symmetrical and asymmetrical cortisol secretion.

Table S2. Linear regression for A/M LI cut-off prediction

Figures

Figure S1. Subtype diagnosis defined with A/C LI with or without cosyntropin stimulation.

Figure S2. Selectivity of unstimulated AVS defined with C-ratio \geq 3 or M-ratio \geq 3.

Figure S3. Selectivity of unstimulated AVS defined with C-ratio \geq 2 or M-ratio \geq 2.

Figure S4. Selectivity of cosyntropin stimulated AVS defined with C-ratio \geq 5 or M-ratio \geq 3.

Table S1. Clinical and biochemical characteristics of patients with symmetrical and asymmetrical cortisol secretion.

Variables	Symmetrical cortisol secretion (n=72)	Asymmetrical cortisol secretion (n=16)	
Age at screening (years)	49±9	52±8	0.222
Female sex, n (%)	23 (31.9)	6 (37.5)	0.669
Systolic BP (mmHg)	158±20	154±20	0.471
Diastolic BP (mmHg)	96±11	94±12	0.480
BMI (Kg/sqm)	27±4	27±3	0.969
Lowest Potassium (mEq/L)	3.5±0.6	3.5±0.7	0.902
Creatinine (mg/dL)	0.90±0.20	0.85±0.21	0.422
Diabetes, n (%)	6 (8.8)	-	0.218
PRA (ng/mL/h)	0.20 (0.10-0.42)	0.30 (0.17-0.51)	0.363
Renin (μU/mL)	1.60 (0.50-3.27)	3.45 (2.90-3.45)	0.193
Aldosterone (ng/dL)	33.2 (24.1-45.2)	38.7 (28.3-49.4)	0.347
Subtype diagnosis (%)			
Unilateral PA	38 (52.8)	12 (75.0)	
Bilateral PA	32 (44.4)	4 (25.0)	
Undetermined	2 (2.8)	-	

Values are mean ± SD, median (IQR), or absolute number (%).

BMI: body mass index; BP: blood pressure; PA: primary aldosteronism; PRA: plasma renin activity.

Table S2. Linear regression for A/M LI cut-off prediction

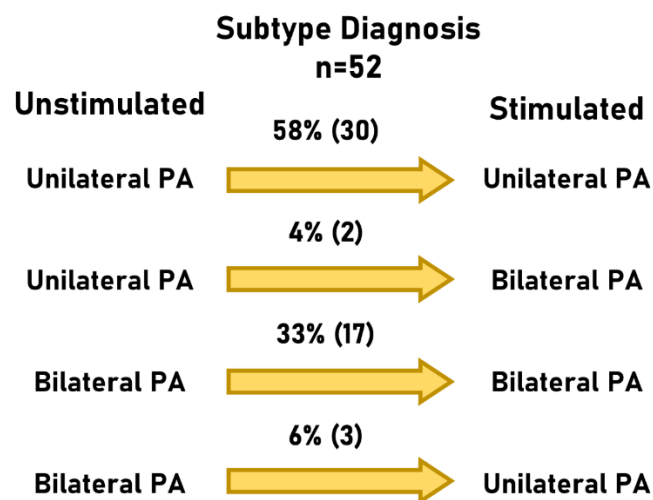
A/M LI	A/C LI
Intercept	-1.022
β Estimate (I.C.)	1.335 (1.254-1.417)
P-value	<0.001

β is expressed as median (IQR). A/M LI cut-off was calculated by the following equation:

$$\text{A/M LI} = -1.022 + (4 \times 1.335) = 4.318.$$

A/C: aldosterone to cortisol lateralization index; A/M: aldosterone to metanephrine lateralization index.

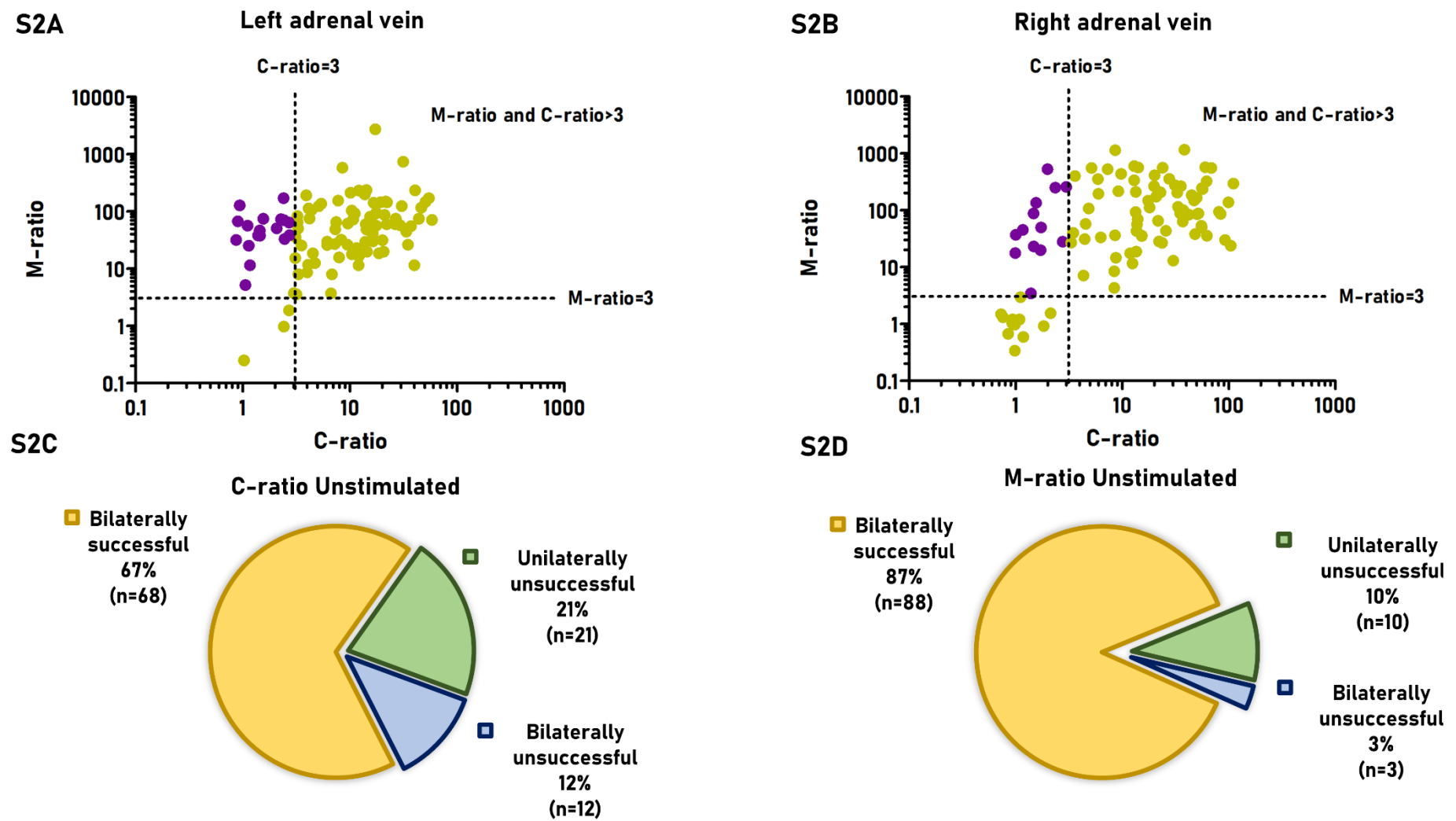
Figure S1. Subtype diagnosis defined with A/C LI with or without cosyntropin stimulation.



The figure shows the changes in subtype diagnosis defined with and without cosyntropin stimulation.

A/C LI, (Aldosterone/Cortisol)_{dominant adrenal vein}/(Aldosterone/Cortisol)_{non dominant adrenal vein}; CR, contralateral ratio; PA, primary aldosteronism.

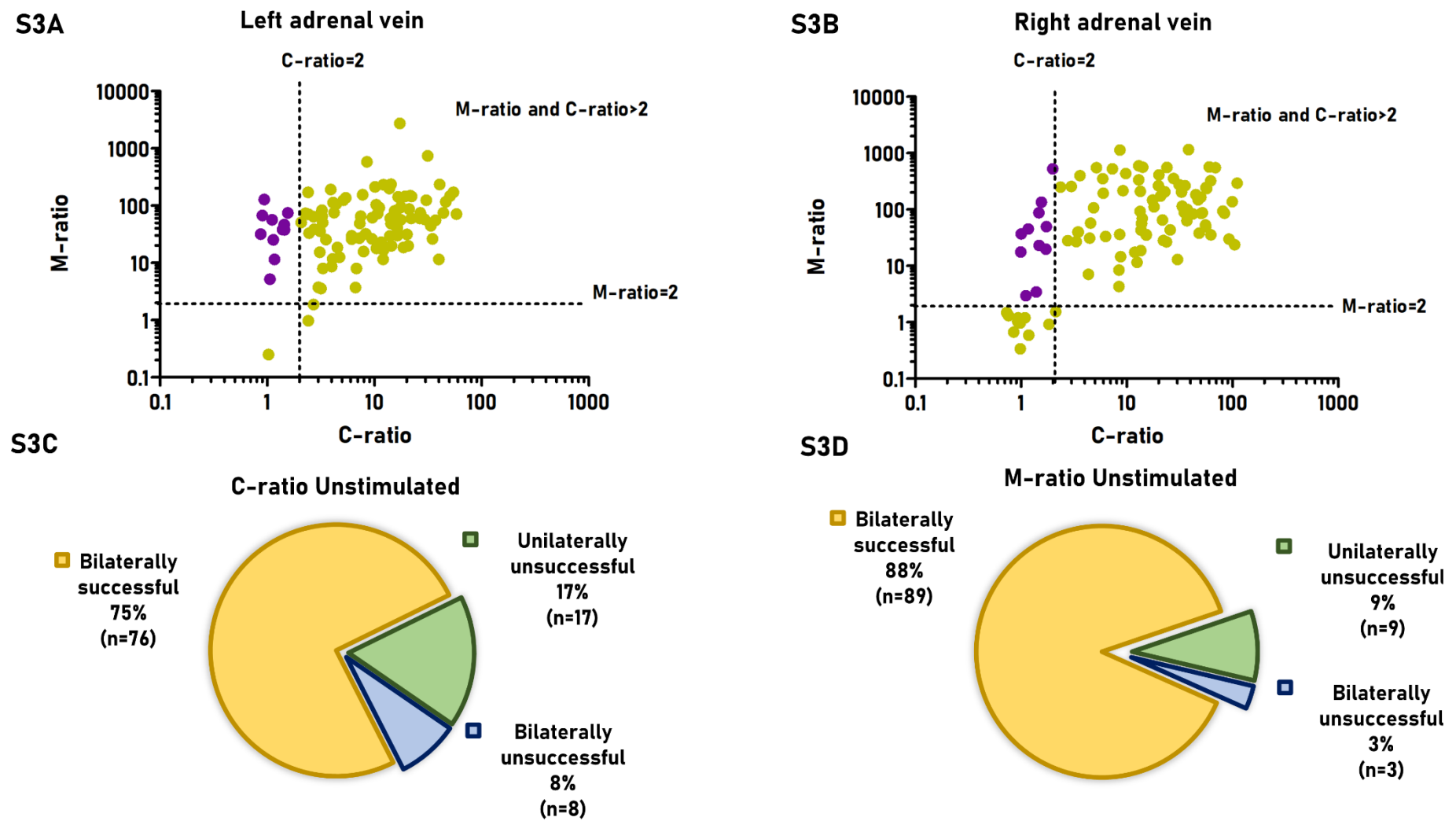
Figure S2. Selectivity of unstimulated AVS defined with $C\text{-ratio} \geq 3$ or $M\text{-ratio} \geq 3$.



The scatterplots show SI defined with C-ratio or M-ratio of unstimulated AVS ($n=101$) in the left adrenal vein (**A**) or right adrenal vein (**B**). Yellow dots indicate adrenal samplings that were defined selective or unselective with both methods (C-ratio and M-ratio). Purple dots indicate adrenal samplings that were defined selective with M-ratio and unselective with C-ratio. The pie charts show the proportion of successful, unilaterally unsuccessful and bilaterally unsuccessful procedures considering $C\text{-ratio} \geq 3$ (**C**) and $M\text{-ratio} \geq 3$ (**D**) as selectivity index.

AVS: adrenal venous sampling; C-ratio: $\text{Cortisol}_{\text{adrenal vein}}/\text{Cortisol}_{\text{peripheral vein}}$; M-ratio: $\text{Metanephrine}_{\text{adrenal vein}}/\text{Metanephrine}_{\text{peripheral vein}}$; SI: selectivity index.

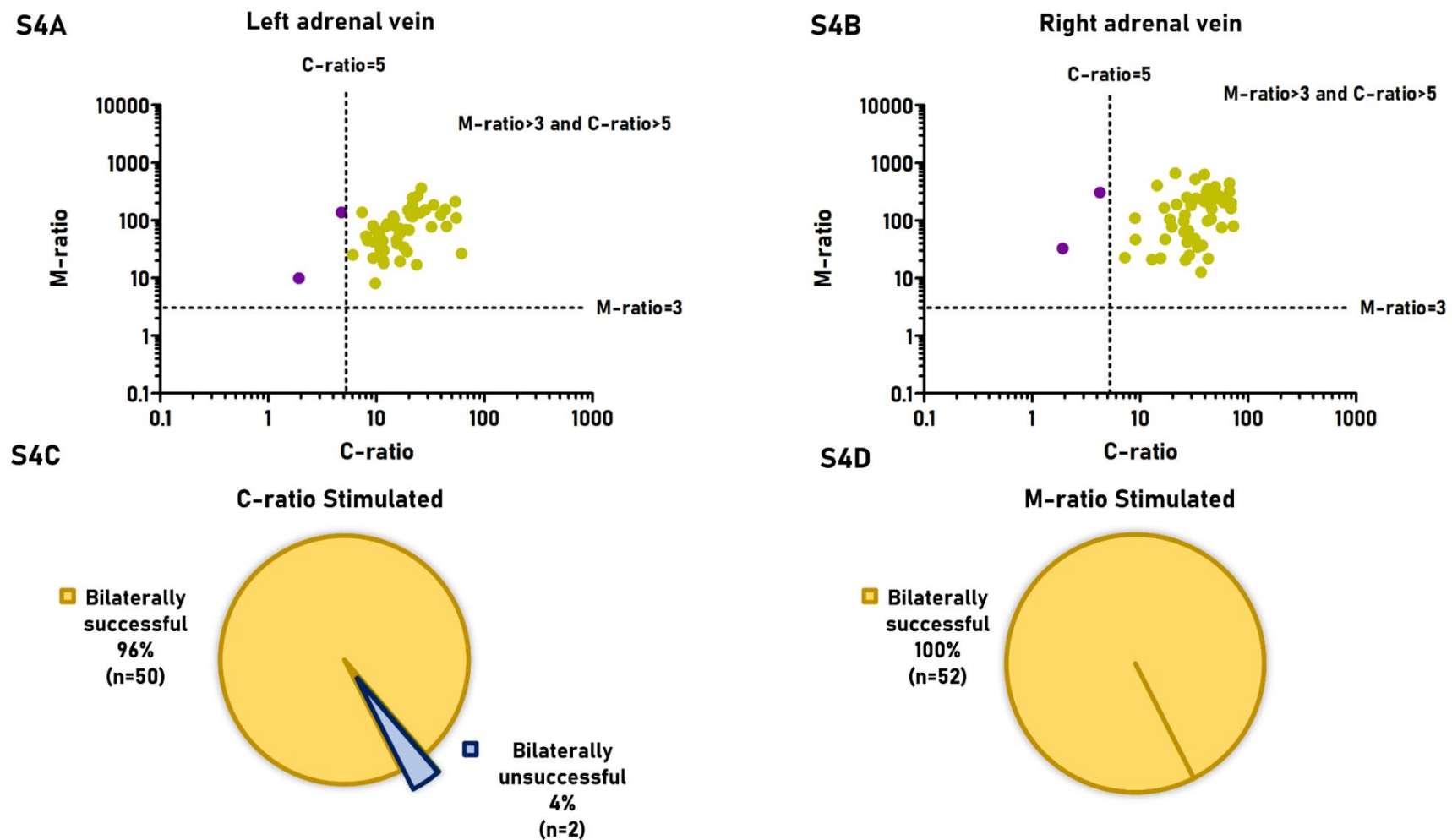
Figure S3. Selectivity of unstimulated AVS defined with $C\text{-ratio} \geq 2$ or $M\text{-ratio} \geq 2$.



The scatterplots show SI defined with C-ratio or M-ratio of unstimulated AVS ($n=101$) in the left adrenal vein (**A**) or right adrenal vein (**B**). Yellow dots indicate adrenal samplings that were defined selective or unselective with both methods (C-ratio and M-ratio). Purple dots indicate adrenal samplings that were defined selective with M-ratio and unselective with C-ratio. The pie charts show the proportion of successful, unilaterally unsuccessful and bilaterally unsuccessful procedures considering $C\text{-ratio} \geq 2$ (**C**) and $M\text{-ratio} \geq 2$ (**D**) as selectivity index.

AVS: adrenal venous sampling; C-ratio: $\text{Cortisol}_{\text{adrenal vein}}/\text{Cortisol}_{\text{peripheral vein}}$; M-ratio: $\text{Metanephrine}_{\text{adrenal vein}}/\text{Metanephrine}_{\text{peripheral vein}}$; SI: selectivity index.

Figure S4. Selectivity of cosyntropin stimulated AVS defined with $C\text{-ratio} \geq 5$ or $M\text{-ratio} \geq 3$.



The scatterplots show SI defined with C-ratio or M-ratio of unstimulated AVS ($n=52$) in the left adrenal vein (**A**) or right adrenal vein (**B**). Yellow dots indicate adrenal samplings that were defined selective or unselective with both methods (C-ratio and M-ratio). Purple dots indicate adrenal samplings that were defined selective with M-ratio and unselective with C-ratio. The pie charts show the proportion of successful, unilaterally unsuccessful and bilaterally unsuccessful procedures considering $C\text{-ratio} \geq 5$ (**C**) and $M\text{-ratio} \geq 3$ (**D**) as selectivity index.

AVS: adrenal venous sampling; C-ratio: $\text{Cortisol}_{\text{adrenal vein}}/\text{Cortisol}_{\text{peripheral vein}}$; M-ratio: $\text{Metanephrine}_{\text{adrenal vein}}/\text{Metanephrine}_{\text{peripheral vein}}$; SI: selectivity index.