

Using a morning cortisol to predict adrenal reserve and guide management.

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Introduction

- The Short Synacthen Test (SST) is the most widely used dynamic assessment of adrenal reserve
- Random basal cortisol levels could provide an alternative screening assessment.
- Large numbers of patients are prescribed glucocorticoids and are at risk of iatrogenic adrenal suppression

Methods

- 3603 SST results were analysed from across all medical specialities (Queen Elizabeth Hospital, Birmingham).
- all SSTs were performed in the morning (09:00 – 12:00)
- Serum cortisol concentrations were analysed by a standard radioimmunoassay (Roche)
- A 30-minute cortisol value ≥ 550 nmol/l was defined as a pass
- Results were divided into groups including age, sex, pituitary & adrenal pathology and patients taking inhaled glucocorticoids
- Receiver Operator Characteristic curves were generated
- We analysed Area Under Curve (AUC) and 'best-fit' cortisol values to predict cut-off values for specificities & sensitivities

Results

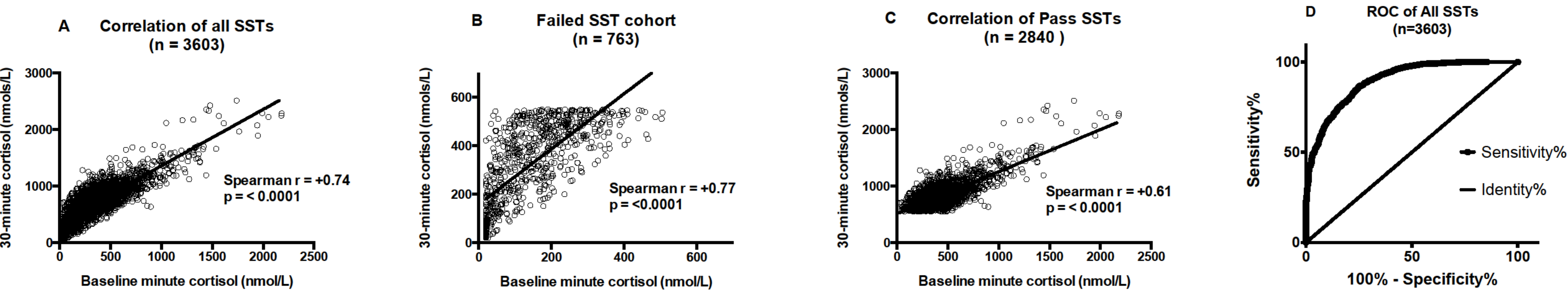


Figure 1: Panel A: Correlation of baseline and 30-minute serum cortisol concentrations, Spearman $r=+0.74$, $p<0.0001$. Panel B: Correlation of baseline and 30-minute serum cortisol in those that failed SST, Spearman $r=+0.77$, $p<0.0001$. Panel C: Correlation in those that passed SST, Spearman $r=+0.61$, $p<0.0001$. Panel D: ROC curve of baseline cortisol as a predictor of passing SST in all patients.

Table 1: The results of SSTs in 3603 patients divided according to indication.

Description of indication	n	%Pass (n)	% Fail (n)
Treatment (current or prior) with inhaled, nasal or topical glucocorticoids	303	66.0 (200)	34.0 (103)
Treatment (current or prior) with oral or intravenous glucocorticoids	202	49.5 (100)	50.5 (102)
Post-operative assessment after pituitary surgery (without radiotherapy)	329	67.8 (223)	32.2 (106)
Post-operative assessment after pituitary surgery (with radiotherapy)	134	81.3 (109)	18.7 (25)
Pituitary adenoma (without surgery or radiotherapy)	330	87.6 (289)	12.4 (41)
Other conditions affecting the pituitary	219	72.1 (158)	27.9 (61)
<i>All Pituitary sub group</i>	<i>1012</i>	<i>77.0 (779)</i>	<i>23.0 (233)</i>
Other tumours of the central nervous system	489	75.9 (371)	24.1 (118)
Adrenal disease (including CAH, Addison's disease & carcinoma)	126	35.0 (44)	65.0 (82)
Investigation of co-existent autoimmune disease	133	88.5 (118)	11.5 (15)
Hyponatraemia or hyperkalaemia	85	89.4 (76)	10.6 (9)
Hypoglycaemia	34	100.0 (34)	0 (0)
Hypotension, syncope and collapse	189	95.2 (180)	4.8 (9)
Fatigue, weight loss and malaise	220	90.4 (199)	9.4 (21)
Other indications or "none" specified (not including critical care)	810	91.2 (739)	8.8 (71)
<i>All SSTs</i>	<i>3603</i>	<i>78.8 (2840)</i>	<i>21.2 (763)</i>
ICU	166	89 (146)	11.0 (18)

Table 2: SST results divided into different categories with AUC, sensitivities & specificities and 'best-fit' (Youden index = max {Sensitivity + Specificity – 100}) for serum cortisol concentrations (nmol/L).

Group	AUC	Youden Index	Specificity			Sensitivity		
			95%	99%	100%	95%	99%	100%
All (n=3603)	0.89 (0.80 - 0.99)	212 (87% sens + 75% spec)	342	441	506	162	107	< 20
Pituitary (n=1012)	0.9 (0.88 - 0.92)	178 (90% sens. + 73% spec.)	314	373	410	150	80	48
Post-op Pituitary (n=329)	0.9 (0.87 - 0.94)	187 (88% sens. + 77% spec.)	298	345	350	158	73	47
Post-op pituitary + radiotherapy (n=134)	0.73 (0.61 - 0.84)	174 (88% sens. + 48% spec.)	371	408	410	145	119	45
Pit tumours medical mgt. (n=330)	0.91 (0.87 - 0.95)	204 (84% sens. + 83% spec.)	246	317	318	154	82	56
Miscellaneous pituitary (n=219)	0.9 (0.85 - 0.95)	170 (91% sens. + 80% spec.)	290	393	397	129	80	52
CNS (n=489)	0.9 (0.86-0.94)	169 (96% sens. + 72% spec.)	397	458	506	159	101	48
Adrenal (n=126)	0.9 (0.86-0.96)	239 (84% sens. + 82% spec.)	320	484	518	185	154	151
ICU (n=166)	0.93 (0.86-1)	367 (90% sens. + 90% spec.)	762	764	765	270	137	117
Inhaled GC's (n=236)	0.91 (0.87 - 0.94)	220 (88% sens. + 75% spec.)	334	358	359	150	64	34
Age < 30 (n=362)	0.87 (0.83 - 0.92)	196 (87% sens+ 71% spec)	397	486	488	156	113	48
Age 30 - 49 (n=1033)	0.89 (0.87-0.92)	211 (81% sens. + 82% spec.)	342	408	505	112	85	51
Age 50 - 69 (n=1202)	0.9 (0.88 - 0.93)	261 (74% sens. + 85% spec.)	325	385	506	165	101	< 20
Age 70 - 100 (n=959)	0.92 (0.90 - 0.94)	294 (82% sens. + 86% spec.)	359	461	467	198	111	34
Men (n=1572)	0.9 (0.88 - 0.92)	208 (90% sens. + 73% spec.)	344	461	505	174	114	< 20
Women (n=1973)	0.89 (0.88 - 0.91)	201 (87% sens. + 74% spec.)	338	411	507	157	91	48
Pre-menopause (n=818)	0.87 (0.84 - 0.9)	201 (82% sens. + 75%spec.)	348	412	459	148	82	49
Post-menopause (n=1155)	0.91 (0.89 - 0.93)	256 (85% sens. + 79% spec.)	331	439	507	169	97	48

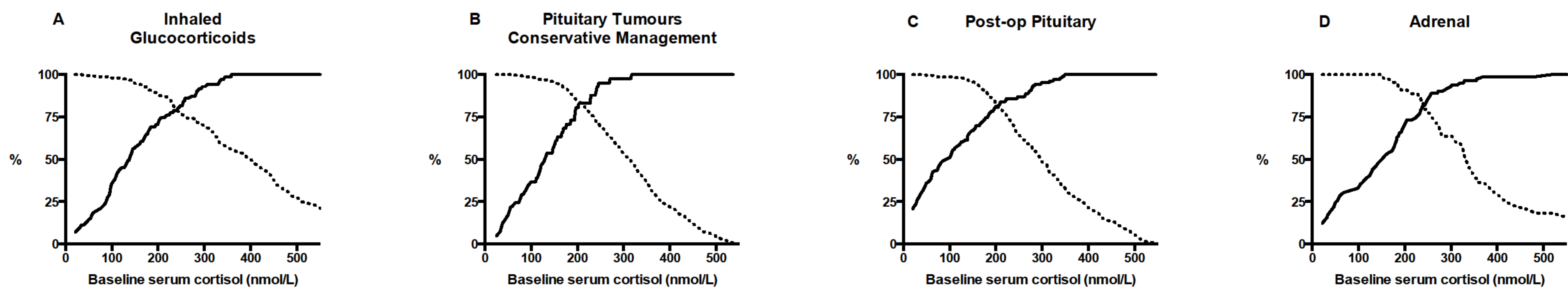


Figure 2: Baseline serum cortisol concentration as a predictor of the 30-minute cortisol concentration during an SST. Baseline serum cortisol concentration is graphed against the % likelihood of passing (specificity = continuous line) or failing (sensitivity = dashed line) the SST. Panel A: Inhaled glucocorticoids. Panel B: Pituitary tumours being conservatively managed. Panel C: Post-operative pituitary. Panel D: Adrenal pathology.

Conclusion

- A high clinical index of suspicion of adrenal insufficiency mandates dynamic assessment of adrenal reserve by SST.
- A basal cortisol may have a clinical utility in discrete patient cohorts, such as those on inhaled glucocorticoids
- In patients prescribed inhaled glucocorticoids, retrospectively applying a cut-off of 359 & 34nmol/L for baseline cortisol concentration, would have avoided 42% of SSTs (n=100).
- In post-op pituitary patients, applying a cut-off of 350 & 47nmol/L would have avoided 30% of SSTs (n=99).
- Baseline cortisol concentrations can be informative in predicting the SST response.