

JOURNAL READING

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POTENTIAL MISDIAGNOSES OF BELL'S PALSY IN THE EMERGENCY DEPARTMENT

INTRODUCTION

- Common presentation:
 - inability to raise eyebrows, wrinkle the forehead, or close the eyelid
 - Loss of the nasolabial fold
 - Loss of the nasolabial fold
 - alterations in taste
- Pathophysiology: inflammation of the facial nerve at the geniculate ganglion
- DDx:
 - stroke
 - Infection: Lyme disease, HIV infection, Ramsey-Hunt syndrome (herpes zoster)
 - diabetes mellitus, sarcoidosis
 - Mass lesion: lymphoma, or cerebellopontine tumors

METHOD

- Corhort Study: Data base(California Office of Statewide Health Planning and Development)
- Inclusion criteria:
 - Date: 2005-2011; Age: >17yr; ED出院診斷ICD-9 351.0
- Primary outcome:
 - 90天內住院或急診診斷為 stroke, ICH, SAH, brain tumor, Guillain-Barre syndrome 等
- Exclusion:
 - DM neuropathy, sarcoidosis等不列入significant misdiagnosis(預後差不多)

Characteristics	No Alternative Diagnosis Made n=43,623		Alternative Diagnosis Made n=356	
	No.	% (95% CI)	No.	% (95% CI)
Age quartile, y				
18-31	10,890	25.0 (24.6-25.4)	70	19.7 (15.9-24.1)
32-44	10,748	24.6 (24.2-25.0)	69	19.4 (15.6-23.8)
45-56	11,339	26.0 (25.6-26.4)	93	26.1 (21.8-30.9)
>57	10,646	24.4 (24.0-24.8)	124	34.8 (30.1-39.9)
Sex				
Male	21,280	48.8 (48.3-49.2)	166	46.6 (41.5-51.8)
Female	22,343	51.2 (50.8-51.7)	190	53.4 (48.2-58.5)
Race				
White	15,164	38.4 (38.0-38.9)	140	41.1 (36.0-46.4)
Black	2,545	6.45 (6.21-6.70)	38	11.1 (8.1-15.1)
Hispanic	17,900	45.4 (44.9-45.9)	134	39.3 (34.3-44.6)
Asian	2,492	6.32 (6.08-6.56)	18	5.28 (3.37-8.19)
Other	1,341	3.40 (3.23-3.58)	11	3.23 (1.81-5.69)
Insurance status				
Medicare	6,845	15.7 (15.4-16.0)	92	25.8 (21.6-30.6)
Medicaid	6,123	14.0 (13.7-14.4)	69	19.4 (15.6-23.8)
Private	19,502	44.7 (44.2-45.2)	117	32.9 (28.2-37.9)
Self-pay	8,725	20.0 (19.6-20.4)	57	16.0 (12.6-20.2)
Other	2,415	5.54 (5.33-5.76)	21	5.90 (3.89-8.85)
Visit day				
Weekday	30,842	70.7 (70.3-71.1)	245	68.8 (63.8-73.4)
Weekend	12,781	29.3 (28.9-29.7)	111	31.2 (26.6-36.2)
Comorbidity				
Hypertension	8,439	19.3 (19.0-19.7)	105	29.5 (25.0-34.4)
Diabetes mellitus	5,169	11.8 (11.6-12.1)	73	20.5 (16.6-25.0)
Coronary heart disease	666	1.53 (1.42-1.65)	6	1.69 (0.78-3.63)
Congestive heart failure	170	0.39 (0.34-0.45)	1	0.28 (0.05-1.57)
Chronic kidney disease	281	0.64 (0.57-0.72)	5	1.40 (0.60-3.24)
Chronic obstructive pulmonary disease	250	0.57 (0.50-0.65)	4	1.12 (0.44-2.85)
Imaging				
CT or MRI	6,149	14.1 (13.8-14.4)	75	21.1 (17.2-25.6)

STATISTIC METHOD

- Survival analysis: 不同時間點發生的misdiagnosis rate,
- End-date: 90 day after 1st visit(index day)或 patient die或診斷確定
- 多種預後影響因子分析 : Multivariable Cox proportional hazards model
- Robust standard error: 計算趨勢取現時刪除極端值的統計方式
- 計算程式: Stata SE

RESULT

- 共收案43979位病人, 年齡中位數: 45 yr(四分位數 32yr, 57yr)
- 在急診有安排影像檢查者:6224(14.2%), CT居多5763(13.2%)
- 90天follow的結果:356(0.8%)發生有意義的misdiagnosis; 127(0.3%)發生致死性的misdiagnosis
- 常見的alternative Dx: ischemic stroke, herpes zoster, Guillain-Barre syndrome, Otitis media
 - 假設alternative Dx是正確診斷
- 與significant misdiagnosis相關的因子
 - 黑人、老人
 - 糖尿病患者
 - Medicaid使用者(社福醫療補助)

Table 2. Multivariate associations between demographics/ comorbidities and alternative diagnosis made on 90-day follow-up for patients with an initial ED diagnosis of Bell's palsy.

Covariates	HR (95% CI)
Age, every 10 y	1.11 (1.01-1.21)
Female sex	1.02 (0.80-1.29)
Race	
White	Reference
Black	1.68 (1.13-2.48)
Hispanic	0.82 (0.62-1.07)
Asian	0.75 (0.45-1.27)
Other	0.90 (0.50-1.64)
Insurance status	
Medicare	Reference
Medicaid	1.26 (0.85-1.87)
Private	0.65 (0.46-0.93)
Self-pay	0.77 (0.52-1.15)
Other	0.84 (0.46-1.55)
Weekend	1.12 (0.89-1.41)
Comorbid conditions	
Hypertension	1.22 (0.94-1.59)
Diabetes	1.46 (1.10-1.95)
Coronary heart disease	0.64 (0.30-1.38)
Congestive heart failure	0.36 (0.49-2.58)
Chronic kidney disease	1.33 (0.54-3.29)
Chronic obstructive pulmonary disease	1.23 (0.45-3.36)
Imaging use (CT or MRI)	1.43 (1.10-1.85)

Table 3. Cumulative counts of alternative diagnoses made on 7-, 14-, 30-, and 90-day follow-up for 356 patients* with an initial ED diagnosis of Bell's palsy.

Diagnosis	Day of Follow-up, No.				%
	7	14	30	90	
Ischemic stroke	53	62	77	98	27.3
Intracranial hemorrhage	4	4	5	10	2.8
Subarachnoid hemorrhage	0	0	0	2	0.6
Brain tumor	0	1	2	4	1.1
Central nervous system infection	4	5	7	13	3.6
HIV infection	3	6	7	19	5.3
Guillain-Barre syndrome	23	30	37	39	10.9
Lyme disease	1	0	0	3	0.8
Otitis media or mastoiditis	20	38	56	86	24.0
Herpes zoster	34	57	69	83	23.2
Total	142	204	261	358	

*Two patients received more than 1 alternative diagnosis.

LIMITATION & DISCUSSION

- 只討論人口學與流病學上的因子發生misdiagnosis的關聯
- 以上資料並沒有包含病史、NE、其他醫療complaint
- 有做CT與MRI呈現與primary outcome正相關，其背後的原因可能就跟上述未呈現的因子有關
- 90天的追蹤interval, 很難確定兩次診斷的醫療事件是相關的
- 作者又說，也有些Bell's palsy的診斷錯誤可能90天後也沒抓到，可以互相抵銷影響(這甚麼鬼推論)
- 10.9%的病人最後診斷為Guillan Barre syndrome，而此診斷有許多種變形
 - AIDP(acute inflammatory demyelinating polyneuropathy): ascending weakness
 - Miller Fisher syndrome: Ophthalmoplegia, ataxia, areflexia(descending weakness)
 - Bickerstaff encephalitis.... etc

COMMENT

- 有提出哪些population要注意: DM, old age.....除此之外好像沒幫助
- 臨床上比較需要的是那些complaint或者sign可以幫助 rule in or rule out Bell's palsy →這篇沒講
- 末尾文章的討論有提及曾有研究指出，就算照會Neuro也有36%診斷不確定或者後來有誤→安慰?

FLUOROQUINOLONES AND THE RISK OF SERIOUS ARRHYTHMIA: A POPULATION-BASED STUDY

INTRODUCTION

- 曾有paper說 quinolones會造成QT prolonged, Torsades de pointes, 或其他嚴重心律不整
- 之前的論文沒有特別針對個別quinolone及confounders做風險討論

METHODS

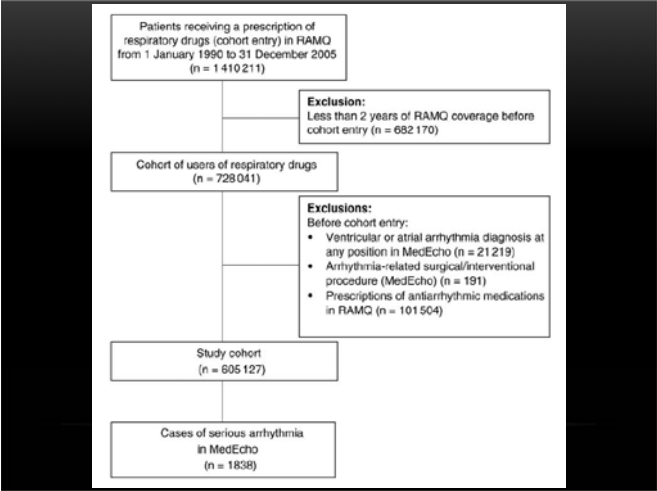
- Cohort study
- 收案: 1990年1月~2005年12月登記在魁北克health care database底下的病人・追蹤其記錄至2007年3月
- 使用nested case-control analysis(嵌入型病例对照研究法)追蹤住院中有嚴重心律不整診斷的病人:
 - 主要用於exposure因子在cohort中發生機會很低或者在不同階層的族群發生率嚴重不一・以統計方法在相同涉險族群中抽取control 組
 - 算是一種case control 精神的統計方式
- 使用Conditional logistic regression計算 fluoroquinolone 造成嚴重心律不整的rate ratio (RR)

METHODS

- 排除條件:
 - 初次使用呼吸道治療藥物時未滿2年保險其者
 - 過去有嚴重心不整併使者
 - 有arrhythmia related 手術或者intervention者・正在使用antiarrhythmia藥物者
- 嚴重心律不整定義:
 - Paroxysmal VT, VF, cardiac arrest
 - 新發生嚴重心律不整定義: (± 3 months from the date of diagnosis做intervention) 或者(± 1 month from the date of diagnosis使用任何心律不整藥物)
- Exposure 定義
 - Current/recent/past: 14天內/ 15~30天/ 31~365天內使用過 quinolone

METHODS

- Covariates
 - 包含CHF, valvular heart dz, 呼吸道疾病, anemia,
 - 藥物: CCB, ACEI, beta-blocker, NSAID
 - COPD:
 - 中等acute exacerbation(AE): 使用口服類固醇和抗生素
 - 嚴重AE: 需要住院者
- 在敏感性分析中排除最近14~28天有住過院的病人(排除time bias?)



RESULT

Table 1. Comparison of Cases of Serious Arrhythmia and Matched Controls

	Cases (n = 1838)	Controls (n = 36 760)			
Age, years, mean $\pm$ SD	75.3 $\pm$ 12.2	75.2 $\pm$ 12.0	Hyperlipidemia, %	9.3	5.1
Follow-up, years, mean $\pm$ SD	5.3 $\pm$ 4.0	5.3 $\pm$ 4.0	Atherosclerosis, %	8.9	3.6
Sex, female, %	56.7	56.7	Renal failure (chronic disease and/or acute episodes), %	13.4	4.0
1 year before the index date			Anemia, %	14.4	7.1
No. of hospitalizations, mean $\pm$ SD	0.3 $\pm$ 0.4	0.2 $\pm$ 0.4	Asthma, %	12.7	10.7
Heart failure, %	34.2	7.2	Thyroid diseases, %	15.9	12.9
Stroke, %	4.3	2.8	Septicemia, %	1.4	0.4
Atrial fibrillation, %	26.3	4.4	Comedications		
Valvular disease, %	8.5	1.7	Antihypertensive drugs, %	80.1	56.2
Coronary artery disease, %	47.6	16.7	Cardiotonic drugs, %	30.6	8.3
Congenital structural cardiovascular abnormalities, %	1.1	0.2	Oral corticosteroids, %	17.7	12.2
Enlarged heart, %	4.4	0.5	Inhaled corticosteroids, %	36.5	33.4
Diabetes, %	20.7	11.4	Other respiratory medications, %	53.7	45.3
Hypertension, %	36.8	28.7	Lipid-lowering drugs, %	18.5	14.2
			Thyroid medications, %	14.2	12.1
			NSAIDs, %	56.8	47.3
			30 days before the index date		
			COPD exacerbation, %		
			Severe (COPD hospitalizations)	7.3	1.5
			Moderate		
			Macrolide and OCS (on the same date)	0.05	0.08
			Nonmacrolide and OCS (on the same date)	1.0	0.6
			Potentially inducing arrhythmia medications, %		
			Antiarrhythmic drugs	5.5	0.8
			Antidepressants	8.7	6.5
			Antiemetic drugs	3.4	1.9
			Antipsychotic drugs	5.5	1.5

RESULT

Table 2. Distribution of Cases of Serious Arrhythmias by Type

	Overall (n = 1838)	With Surgical/Interventional Procedure ^a (n = 121)	With Pharmacotherapy ^b (n = 272)
Nonfatal cases, No. (%)	1209 (65.8)	117 (96.7)	270 (99.3)
Paroxysmal ventricular tachycardia	512 (27.9)	80 (66.1)	106 (39.0)
Cardiac arrest	160 (8.7)	8 (6.6)	47 (17.3)
Ventricular fibrillation and/or flutter	92 (5.0)	12 (9.9)	29 (10.7)
Unspecific arrhythmia	445 (24.2)	17 (14.0)	88 (32.4)
Fatal cases, No. (%)	629 (34.2)	2 (1.7)	2 (0.7)
Paroxysmal ventricular tachycardia	33 (1.8)	---	---
Cardiac arrest	395 (21.5)	1 (0.8)	---
Ventricular fibrillation and/or flutter	55 (3.0)	---	---
Unspecific arrhythmia	91 (5.0)	---	---
Sudden or unattended death ^c	55 (3.0)	1 (0.8)	2 (0.7)

RESULT

Table 3. Crude and Adjusted Rate Ratios of Serious Arrhythmia for Current, Recent, and Past Use of Fluoroquinolones

	Cases (n = 1838)	Controls (n = 36 670)	Crude RR	Adjusted RR (95% CI) ^a
Recency of use, No. (%) ^b				
Current, new	20 (1.1)	215 (0.6)	2.04	1.62 (0.97–2.71)
Current, not new	18 (1.0)	229 (0.6)	1.75	1.12 (0.66–1.89)
All current	38 (2.1)	444 (1.2)	1.89	1.34 (0.92–1.93)
Moxifloxacin	7 (0.4)	67 (0.2)	2.40	1.82 (0.79–4.22)
Levofloxacin	5 (0.3)	69 (0.2)	1.66	0.78 (0.29–2.13)
Ciprofloxacin	20 (1.1)	245 (0.7)	1.78	1.32 (0.80–2.18)
Gatifloxacin	4 (0.22)	17 (0.05)	5.69	3.97 (1.15–13.62)
Others	2 (0.1)	46 (0.1)	0.93	0.83 (0.19–3.60)
Recent	30 (1.6)	398 (1.1)	1.68	1.24 (0.82–1.86)
Past	332 (18.1)	4778 (13.0)	1.53	1.14 (1.00–1.32)
Unexposed	1438 (78.2)	31 140 (84.7)	Reference	Reference

RESULT(砍掉了CURRENT住院者)

Table 4. Crude and Adjusted Rate Ratios of Serious Arrhythmia for Current, Recent, and Past Use of Fluoroquinolones

	Cases (n = 1649)	Controls ^a (n = 36 051)	Crude RR	Adjusted RR (95% CI) ^b
Recency of use, No. (%) ^c				
Current, new	18 (1.1)	186 (0.5)	2.37	2.23 (1.31–3.80)
Current, not new	17 (1.0)	206 (0.6)	2.08	1.41 (0.82–2.44)
All current	35 (2.1)	392 (1.1)	2.22	1.76 (1.19–2.59)
Moxifloxacin	7 (0.4)	56 (0.2)	3.30	3.30 (1.47–7.37)
Levofloxacin	3 (0.2)	61 (0.2)	1.30	1.29 (0.40–4.17)
Ciprofloxacin	19 (1.2)	216 (0.6)	2.15	2.15 (1.34–3.46)
Gatifloxacin	4 (0.24)	15 (0.04)	7.40	7.38 (2.30–23.70)
Others	2 (0.1)	44 (0.1)	1.05	1.05 (0.25–4.33)
Recent	26 (1.6)	372 (1.1)	1.70	1.26 (0.80–1.93)
Past	296 (17.9)	4647 (12.9)	1.53	1.15 (1.00–1.34)
Unexposed	1293 (78.4)	30 640 (85.0)	Reference	Reference

LIMITATION& COMMENT

- 作者：
 - 心律不整不會每個都被正確的放在診斷碼，所以有可能被低估
 - 作者有把心律不整不同整段碼做RR評估，結果仍然有意義，所以認為放錯診斷碼的事情不太影響到這篇的結論。
- 可能還有其他covariates會影響到，但他沒想到
- 在新使用以及有持續性使用的患者間，蒐集的研究數據沒有統計意義，所以不知道是不是剛使用時比較危險。
- 最後他終於承認這篇研究只能用在有過呼吸道藥物的病人身上

LIMITATION& COMMENT

- 為什麼要限制再用過呼吸治療藥物的患者呢？
 - Fluoroquinolone用途不止COPD AE吧...
- 用immeasurable time bias來砍patient sample有點牽強，像是在做Data
 - 這個bias主要是在可能同一病症反覆住院，每次治療protocol不太依樣，怕上次住院會干擾到。但這邊沒有提到他砍掉的是怎樣的住院診斷。
- 後面講了很多分子層面的，感覺在拖篇幅，重點是很多病人用quinolone就不是COPD吧~
- 之前有心律不整者也被剔除不加討論，但就是這些人的用藥會讓人比較concern才對