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Hyperparathyroidism & Stroke systematic review + meta-analysis

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Disclosures



The authors declare no conflicts of interest or competing financial incentive.







Background



- PTH: increases blood calcium level by acting on bone, kidneys and intestine.
- PTH also acts on the endothelium and the myocardium. Excess can lead to: ↑ vascular stiffness + calcification; hypertension; ↑ cardiac contractility
- Recent systematic review and meta-analysis have concluded that excess PTH is linked to increased cardiovascular mortality.



Could excess PTH be similarly linked to risk of stroke?







Rationale



- Why do we care?
 - Stroke is a leading cause of mortality and morbidity.
 - Hyperparathyroidism is a common and treatable condition.
- Studies available in current literature report inconsistent results regarding association between stroke and PTH.

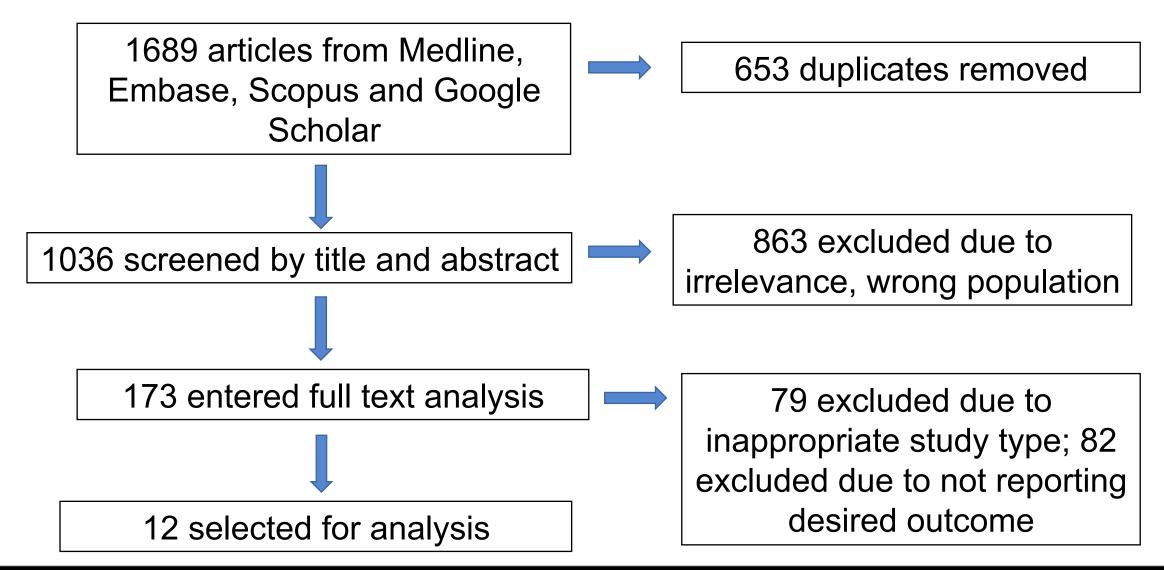
 Systematic review and meta-analysis can help elucidate the connection through enhanced statistical power from large combined sample size.







Method



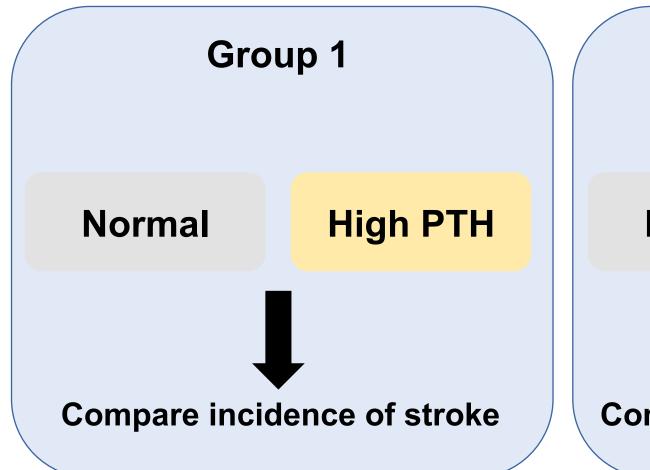


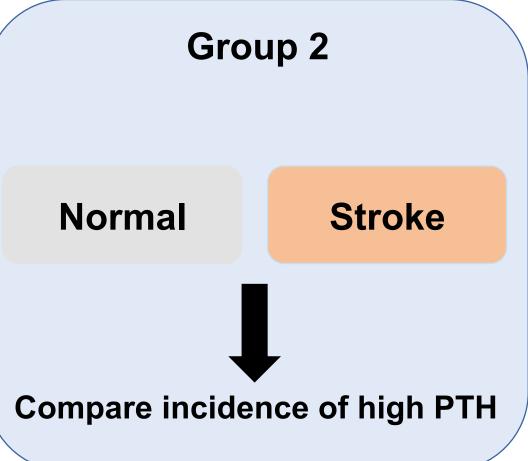




Selected studies













Selected studies



Group 1 (size 96,459)

| First author | Year | Total size | Study type | NOS |
|---------------|------|---------------|------------------|-----|
| Korada | 2016 | 1,703 | Cohort | 8 |
| Kontogeorg os | 2015 | 608 | Cohort | 7 |
| Tagawa | 2014 | 65,849 | Longitudin al | 8 |
| Folsom | 2014 | 10,392 | Cohort | 8 |
| Yu | 2011 | 8,544 | Cohort | 8 |
| Anderson | 2011 | 9,369 | Cohort | 7 |

Group 2 (size 2153)

| First author | Year | Total size | Study type | NOS |
|-----------------|------|-----------------|---------------------|-----|
| Celik | 2017 | 200 | Case control | 8 |
| Tan | 2017 | 404 Case contro | | 7 |
| Kuyumucu | 2014 | 1078 | Case control | 9 |
| Gupta | 2014 | 143 | Cross- sectional | 9 |
| Altay | 2013 | 114 | Case control | 4 |
| Sato | 2003 | 214 | Case control | 8 |





Statistical analysis Group 1



| Study name | <u>s</u> | Statistics for each study | | <u>y</u> | Hazard ratio and 95% CI | | | |
|-------------------------------|-----------------|---------------------------|----------------|------------|-------------------------|--------------|--|--|
| | Hazard ratio | Lower limit | Upper limit | p-Value | | | | |
| Folsom 2014 | 0.99 | 0.82 | 1.19 | 0.916 | | | | |
| Yu 2011 | 3.51 | 2.82 | 4.37 | 0.000 | | | | |
| Anderson 2011 | 1.01 | 0.62 | 1.64 | 0.968 | | | | |
| | 1.53 | 0.60 | 3.91 | 0.372 | | | | |
| l ² =97.45, p<0.00 | 1 No pu | blication bia | as detected | d (p=0.98) | 0.1 0.2 | 0.5 1 2 5 10 | | |

Haemorrhagic

Korada 2016 Kontogeorgos 2015 Tagawa 2014

 $I^2=0.00$, p=0.92

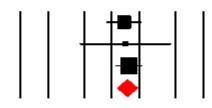
Statistics for each study

| Odds ratio | Lower limit | Upper limit | p-Value |
|---------------|----------------|----------------|---------|
| 1.37 | 0.88 | 2.13 | 0.163 |
| 1.41 | 0.45 | 4.44 | 0.557 |
| 1.54 | 1.10 | 2.16 | 0.013 |
| 1.47 | 1.13 | 1.91 | 0.004 |

No publication bias detected (p=0.71)

Statistics for each study

Odds ratio and 95% CI



0.1 0.2 10

Ischaemic

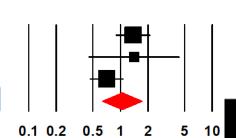
Odds Lower Upper ratio lim it lim it Korada 2016 2.13 1.37 0.88 Kontogeorgos 2015 1.41 4.44 0.45 Tagawa 2014 0.71 0.46 1.09 1.04 0.62 1.74 0.886

I²=57.85, p=0.09

p-Value 0.163 0.557 0.117

No publication bias detected (p=0.79)

Odds ratio and 95% CI







Statistical analysis Group 2



| Study name | | Statistics for each study | | | | dds ra | tio and | 95% (| CI |
|-----------------------------|---------------|---------------------------|-----------------|-------------|------|--------|---------|-------|-----|
| | Odds ratio | Lower limit | Upper lim it | p-Value | | | | | |
| Celik 2017 | 2.66 | 1.43 | 4.95 | 0.002 | | | - | - | |
| Tan 2017 | 230.48 | 137.43 | 386.54 | 0.000 | | | | | |
| Kuyumcu 2014 | 1.19 | 0.82 | 1.72 | 0.359 | | | | | |
| Gupta 2014 | 1.66 | 0.91 | 3.02 | 0.096 | | | | . | |
| Altay 2013 | 2.13 | 1.08 | 4.18 | 0.029 | | | - | F | |
| Sato 2003 | 4.14 | 2.50 | 6.86 | 0.000 | | | | | |
| | 4.70 | 0.91 | 24.20 | 0.064 | | | | | |
| I ² =98.28, p<0. | 001 N | lo publication | n bias detect | ed (p=0.72) | 0.01 | 0.1 | 1 | 10 | 100 |

| Study name | | Statistics for each study | | | Odds ratio and 95% CI |
|-------------------------------|---------------|---------------------------|----------------|-------------|-----------------------|
| | Odds ratio | Lower limit | Upper limit | p-Value | |
| Celik 2017 | 2.66 | 1.43 | 4.95 | 0.002 | |
| Kuyumcu 2014 | 1.19 | 0.82 | 1.72 | 0.359 | + |
| Gupta 2014 | 1.66 | 0.91 | 3.02 | 0.096 | |
| Altay 2013 | 2.13 | 1.08 | 4.18 | 0.029 | |
| Sato 2003 | 4.14 | 2.50 | 6.86 | 0.000 | |
| | 2.12 | 1.30 | 3.47 | 0.003 | |
| I ² =76.22, p=0.00 | 2 N | o publication | bias detecte | ed (p=0.34) | 0.1 0.2 0.5 1 2 5 10 |







Strengths, limitation and the future





Strengths:

- Good quality of studies overall
- Good population size
- No publication bias detected

Limitations:

- Substantial statistical heterogeneity limits interpretation
- Causal relationship between PTH and stroke could not be established

Future studies should assess:

- Effect of PTH on ischaemic stroke compared to haemorrhagic stroke, as well as fatal compared to non-fatal events
- Stratified meta-analysis by gender, age and race may be of clinical interest









Conclusion



