Treatment of chronic Q fever: data from a nationwide cohort study

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Background

Chronic infection with *C. burnetii* (chronic Q fever) is accompanied by high risk for complications and disease-related mortality. Treatment consists of 18 months tetracycline and hydroxychloroquine, with tetracycline plus quinolone as potential alternative choice. However, evidence on effectivity is scarce and toxicity of treatment is high. Therefore, there is need for evidence of effectivity and toxicity of first choice and alternative treatment strategies.

Aim

[1] To compare efficacy of different treatment strategies for chronic Q fever;
[2] To assess toxicity of different treatment strategies for chronic Q fever.

Methods:

Observational, retrospective, cohort study (National Dutch chronic Q fever database).

Time-varying Cox proportional hazards analysis with lagtime (4 weeks).

Domain: patients with proven or probable chronic Q fever, treated with antibiotics.

Determinant: TET/HCQ (reference) vs. TET/QNL vs. QNL vs. TET*.

Outcomes:

- Primary: all-cause mortality;
- Secondary: first disease-related event (complication or chronic Q fever-related mortality)*;
- Secondary: Therapy failure (new complication, chronic Q fever-related mortality, new positive PCR or persistent positive PCR).

*TET=Tetracycline. QNL=Quinolone. HCQ=Hydroxychloroquine. Complications and Q-fever related mortality assessed baesd on predefined criteria.

Flowchart 1. baseline characteristics

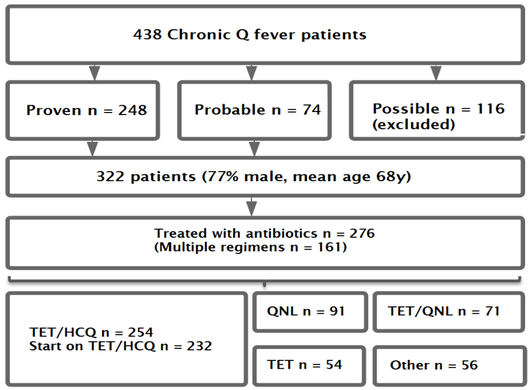

Table 1. Baselinecharacteristics and events

	All patients	Proven chronic Q fever	Probable chronic Q fever
Number of treated patients (%)	276	227	49
Mean age (sd)	68 (12)	69 (12)	66 (12)
Male gender (%)	219 (79)	178 (78)	41 (84)
Vascular focus (%)	146 (53)	121 (53)	25 (51)
Endocarditis focus (%)	62 (22)	55 (24)	7 (14)
Endocarditis & vascular focus (%)	40 (14)	37 (16)	3 (6)
Other focus (%)	28 (10)	14 (6)	14 (29)
Mean follow-up in years (sd)	3.6 (2.2)	3.5 (2.1)	4.0 (2.2)
Deceased (%)	91 (33)	82 (36)	9 (18)
Death related to chronic Q fever (%)	65 (24)	60 (26)	5 (10)
Median time to death from diagnosis in years (IQR)	1.1 (0.2-2.3)	1.0 (0.2 - 2.2)	2.3 (0.6-2.6)
Complications (%)	127 (46)	122 (54)	5 (10)
Disease-related event (%)	154 (56)	145 (64)	9 (18)
Therapy failure during treatment (%)	130 (47)	123 (54)	7 (14)

Results

TET/QNL was associated with a low risk for all-cause mortality (HR0.27, 95%CI0.13-0.58), disease-related events (HR0.44, 95%CI 0.24-0.80) and therapy failure (HR0.40, 95%CI 0.22-0.71), compared to TET/HCQ. QNL was associated with low hazard for secondary outcomes *(table 2)* . TET monotherapy was not associated with any of the outcomes. TET plus HCQ (n=110, 43%) and TET plus QNL (n = 24, 34%) were frequently discontinued due to side effects, QNL monotherapy (n = 27, 29%) and TET monotherapy (n = 32, 59%) were frequently discontinued due to insufficient clinical response.

Conclusion

- ✓ TET/QNL appears to be a safe alternative if TET/HCQ cannot be tolerated, e.g. due to side effects;
- ✓ Definite conclusions regarding QNL monotherapy are difficult to draw due to potential confounding by indication. Frequent alterations due to insufficient response were observed, suggesting insufficient efficacy;
- ✓ High toxicity and discontinuation rate during treatment with TET/HCQ was observed;
- ✓ A strength of this study is the large number of patients (earlier at most 35 patients have been studied) and the use of a model incorperating all treatment strategies within patients;
- ✓ A drawback of this study is the observational nature, which may lead to confounding by indication.

Figure 1. Treatment timelines (weeks) for individual patients, demonstrating high heterogeneity and variation

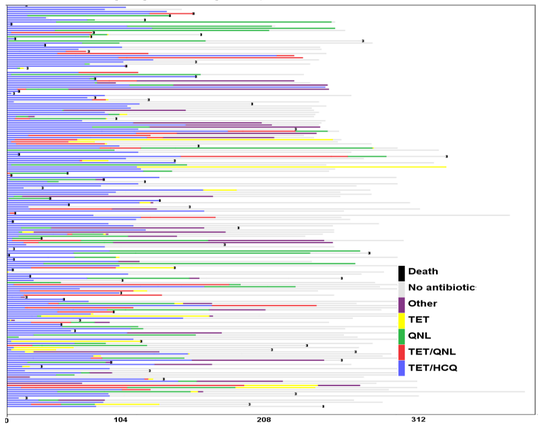

Table 2. Primary and secondary outcomes with corresponding (subdistribution) hazard ratios.

	HR	95% CI	P-value
Ref: TET/HCQ	1.00	n/a	n/a
All-cause mortality			
TET/QNL	0.27	0.13-0.58	<0.001
QNL	0.53	0.27-1.07	0.09
Disease-related events	**SHR**		
TET/QNL	0.44	0.24-0.80	<0.01
QNL	0.46	0.25-0.83	<0.01
Therapy failure	**SHR**		
TET/QNL	0.40	0.22-0.71	<0.01
QNL	0.36	0.21-0.62	<0.001

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