

Avoiding the Burn: Malignant Hyperthermia Risk and Perioperative Management in a Pediatric Patient with RYR1-Positive Family History

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BACKGROUND

- Malignant Hyperthermia (MH) is a potentially life-threatening, pharmacogenetic hypermetabolic disease state, precipitated by volatile anesthetics or succinylcholine.
- The clinical presentation includes rapid onset of hypercarbia, muscle rigidity, hyperthermia, acidosis, and rhabdomyolysis, which can progress to multiorgan failure and death if not promptly recognized and treated.
- MH is primarily linked to dysregulated calcium homeostasis in skeletal muscle, most commonly due to pathogenic variants in the ryanodine receptor-1 (RYR1) gene.
- Estimated genotype prevalence of 1:400 exceeds clinical MH incidence revealing an incomplete penetrance and various modifying factors

CASE DESCRIPTION

- 6-year-old male presented with hematochezia and abdominal pain. A Meckel's diverticulum was found on nuclear imaging
- Maternal RYR1 variant of uncertain pathogenicity; patient without any previous history of genetic testing for RYR1 mutation
- No prior surgical history and no previous exposure to volatile anesthetics or succinylcholine

CLINICAL COURSE

- Preoperative plan: Dantrolene availability verified
- MH-safe workstation prep was completed including: removal of vaporizers, a new circuit, high fresh gas flows, and charcoal filters applied; succinylcholine was removed from room
- Anesthetic technique: Trigger-free TIVA with propofol (induction/maintenance), rocuronium for neuromuscular blockade, fentanyl for analgesia; no volatile agents were utilized
- Procedure: Exploratory laparotomy with small-bowel resection (13 cm segment containing Meckel's diverticulum)
- Outcome: Stable intraoperative parameters without hypermetabolic signs indicative of malignant hyperthermia; uneventful emergence and postoperative course; discharged in stable condition

Figure 1.³ Age distribution at the time of malignant hyperthermia (MH) crisis by sex, in MH probands carrying ryanodine receptor 1 mutations

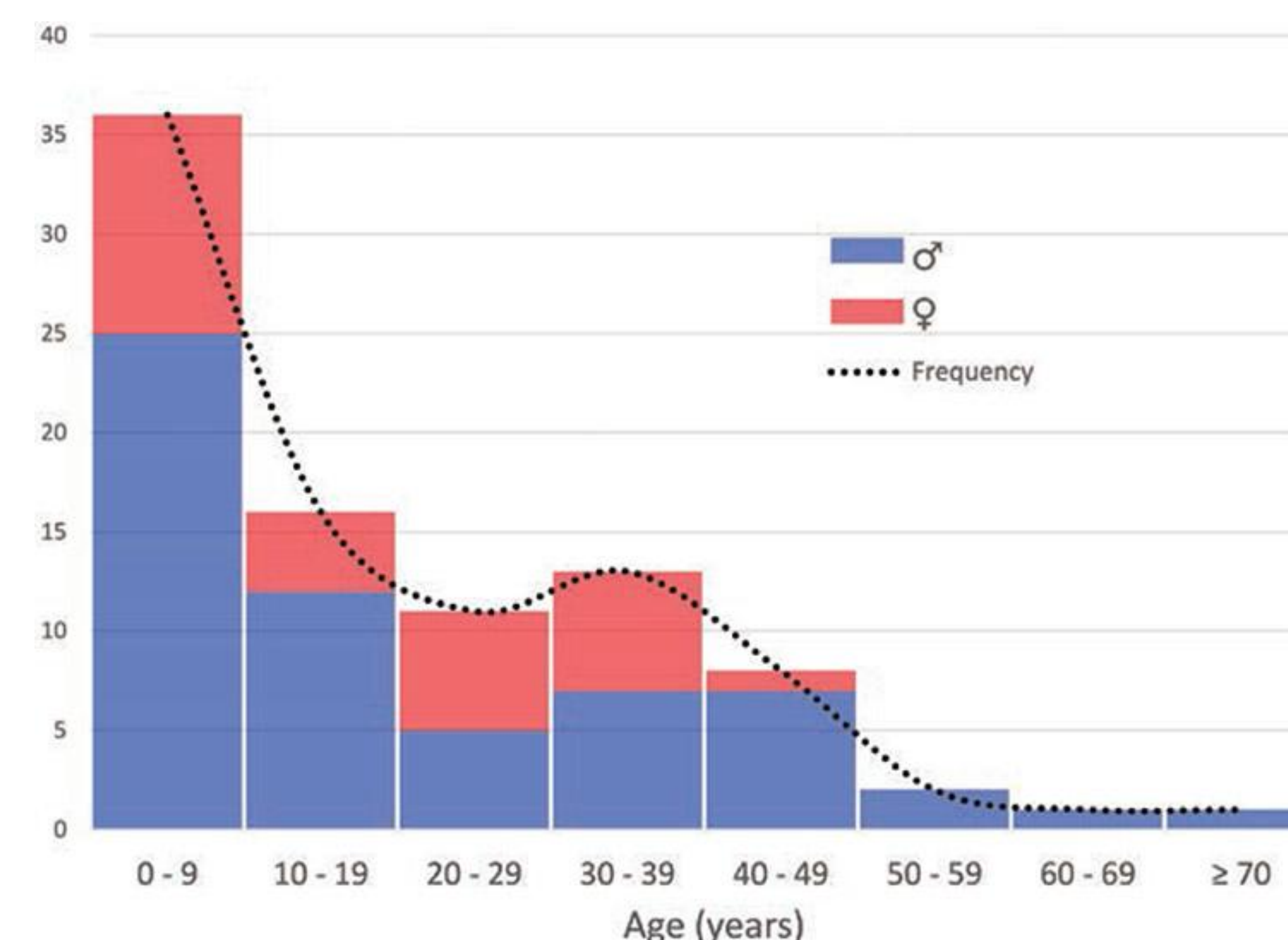


Figure 2.³ An Assessment of Penetrance and Clinical Expression of Malignant Hyperthermia in Individuals Carrying Diagnostic Ryanodine Receptor 1 Gene Mutations

RYR1 mutation	Males		Females	
	Proband	Relative	Proband	Relative
p.Gly341Arg	8	6	3	11
p.Arg614Cys	18	15	12	18
p.Arg614Leu	3	2	2	1
p.Thr2206Met	11	19	6	17
p.Arg2336His	2	2	1	3
p.Ala2350Thr	3	2	0	2
p.Gly2375Ala	4	3	0	4
p.Gly2434Arg	9	4	3	5
p.Arg2454His	4	9	3	10
N	62	62	30	71
# Exposures	87	110	34	126
Penetrance	50 ± 0.11*		29.7 ± 0.18	
Exposures	1 [1-1]		1 [1-1]	
P _{MH-all}	0.31 ± 0.09		0.19 ± 0.12	
P _{MH-probands}	0.71 ± 0.16		0.88 ± 0.14	

Sex data were missing in one proband and three relatives. Penetrance and P_{MH} are expressed as mean ± SD; Exposures as median [interquartile range]. MH, malignant hyperthermia; RYR1, ryanodine receptor 1.
*P < 0.01.

DISCUSSION

- Prevalence of pathogenic RYR1 variants is greater than the frequency of MH events, indicating incomplete penetrance and additional modifiers; genotype does not always predict phenotype
- Autosomal dominant is most common inheritance pattern but autosomal recessive and de novo variants occur; family risk assessment is nuanced, and uncertain status relatives can be managed as MH-susceptible
- Higher penetrance is noted in males with a median reaction age of 12 years old
- A detailed family medical history and anesthesia history improves assessment of malignant hyperthermia risk
- Document prior anesthetic exposures, and consider genetic counseling and testing when feasible
- Adoption of a risk stratified approach that emphasizes preoperative identification and systems readiness in pediatric patients, especially in boys with a family history of RYR1 variants

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