Cardiovascular abnormality in heat stroke

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## Department of Cardiology
### Practical performance

<table>
<thead>
<tr>
<th>Year</th>
<th>2012</th>
<th>2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatient (daily)</td>
<td>23,713 (79.0%)</td>
<td>22,432 (75.8%)</td>
</tr>
<tr>
<td>Inpatient</td>
<td>13,391</td>
<td>12,306</td>
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<tr>
<td>Cardiac catheterization(PCI)</td>
<td>982 (291)</td>
<td>887 (252)</td>
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<tr>
<td>Percutaneous peripheral intervention</td>
<td>89</td>
<td>67</td>
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<tr>
<td>Catheter ablation</td>
<td>94</td>
<td>93</td>
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<tr>
<td>ICD/CRT implantation</td>
<td>54</td>
<td>44</td>
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<tr>
<td>Coronary CT</td>
<td>550</td>
<td>446</td>
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<tr>
<td>Ultrasonic cardiography</td>
<td>7536</td>
<td>7551</td>
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<tr>
<td>Treadmill test</td>
<td>639</td>
<td>491</td>
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<tr>
<td>Holter ECG</td>
<td>388</td>
<td>412</td>
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</tbody>
</table>
Heat illness: Epidemiology

![Graph showing heat illness cases by year (2010-2014) and age groups (0-7y.o., 7-19y.o., 20-64y.o., >65y.o.). The graph indicates a decrease in cases from 2010 to 2014. A pie chart shows the distribution of heat illness cases among different age groups, with 46% in 0-7y.o., 39% in 7-19y.o., 14% in 20-64y.o., and 1% in >65y.o. cases. Each age group is color-coded for clarity.]

- **2010**: 1800 cases
- **2011**: 1600 cases
- **2012**: 1400 cases
- **2013**: 1200 cases
- **2014**: 1000 cases

**Age distribution**:
- **0-7y.o.**: 46%
- **7-19y.o.**: 39%
- **20-64y.o.**: 14%
- **>65y.o.**: 1%
Global warming
Heat stroke

<Definition>
Severe illness characterized by a core temperature >40°C and central nervous system abnormalities such as delirium, convulsions, or coma resulting from exposure to environmental heat or strenuous physical exercise.

<Classification>
Classic: primary occurs in compromised individuals during annual heat waves.
Exertional: in young fit individuals performing strenuous physical exercise.
Thermoregulation

Skin blood vessels dilate: capillaries become flushed with warm blood; heat radiates from skin surface

Body temperature decreases: blood temperature declines and hypothalamus heat-loss center "shuts off"

Sweat glands activated: secrete perspiration, which is vaporized by body heat, helping to cool the body

Blood warmer than hypothalamic set point

Activates heat-loss center in hypothalamus

Stimulus: Increased body temperature (e.g., when exercising or the climate is hot)

Body temperature increases: blood temperature rises and hypothalamus heat-promoting center "shuts off"

Skeletal muscles activated when more heat must be generated; shivering begins

Imbalance

Homeostasis = normal body temperature (35.6°C–37.8°C)

Blood cooler than hypothalamic set point

Activates heat-promoting center in hypothalamus

Stimulus: Decreased body temperature (e.g., due to cold environmental temperatures)
Progression of heat stress to heat stroke

Mediators related to progression to MOF

ECG changes in patients with heat stroke

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Heat Stroke Patients (N = 46)</th>
<th>Probability p Value</th>
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</thead>
<tbody>
<tr>
<td>Sinus tachycardia*</td>
<td>20 (43)</td>
<td>0.05</td>
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<tr>
<td>Atrial fibrillation</td>
<td>4 (8.6)</td>
<td>0.4</td>
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<tr>
<td>Supraventricular tachycardia</td>
<td>2 (4.3)</td>
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<tr>
<td>Bradycardia</td>
<td>2 (4.3)</td>
<td>0.5</td>
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<td>Increased P-R interval</td>
<td>2 (4.3)</td>
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<tr>
<td>Increased Q-T interval</td>
<td>28 (61)</td>
<td>0.007</td>
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<tr>
<td>Conduction defect</td>
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<tr>
<td>Right bundle branch block</td>
<td>4 (8.6)</td>
<td></td>
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<tr>
<td>Intraventricular conduction defect</td>
<td>6 (13)</td>
<td>0.046</td>
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<tr>
<td>Left bundle branch block</td>
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<td>“U” wave</td>
<td>6 (13)</td>
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<tr>
<td>Nonspecific</td>
<td>12 (26)</td>
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<td>Diffuse ST-T changes</td>
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<tr>
<td>Myocardial ischemia</td>
<td>10 (21)</td>
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<tr>
<td>Acute myocardial infarction</td>
<td>4 (8.6)</td>
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<tr>
<td>Old myocardial infarction</td>
<td>2 (4.3)</td>
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</table>

*χ² test; Fisher's Exact Test.
Table 2—Hemodynamic Data for Ten Patients With Heat Stroke*

<table>
<thead>
<tr>
<th>Patient</th>
<th>MAP (85-95 mm Hg)†</th>
<th>RAP (2-5.0 mm Hg)†</th>
<th>CO (ml/min/m²)†</th>
<th>CI (2.5-4.0 ml/min/m²)†</th>
<th>PCWP (5-12 mm Hg)†</th>
<th>MPA (9-18 mm Hg)†</th>
<th>SVR (1,100-1,500 dynes·cm⁻²)†</th>
<th>PVR (120-250 dynes·cm⁻²)†</th>
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<tr>
<td>1</td>
<td>60</td>
<td>1</td>
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<td>6</td>
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<td>7</td>
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<td>7</td>
<td>16</td>
<td>13</td>
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<td>8</td>
<td>53</td>
<td>8</td>
<td>3.1</td>
<td>1.5</td>
<td>11</td>
<td>13</td>
<td>15</td>
<td>1,161</td>
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<tr>
<td>9</td>
<td>90</td>
<td>1</td>
<td>10.6</td>
<td>5.3</td>
<td>4</td>
<td>9</td>
<td>8</td>
<td>770</td>
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<td>10</td>
<td>80</td>
<td>11</td>
<td>8.2</td>
<td>3.0</td>
<td>13</td>
<td>15</td>
<td>21</td>
<td>634</td>
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<tr>
<td>Mean</td>
<td>65</td>
<td>6</td>
<td>8.2</td>
<td>4.4</td>
<td>10</td>
<td>14</td>
<td>17</td>
<td>684</td>
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</table>

*CO = cardiac output; HR = heart rate; MAP = mean arterial pressure; MPA = mean pulmonary artery pressure; PCWP = pulmonary capillary wedge pressure; PVR = pulmonary vascular resistance; RAP = right atrial pressure.
†Values in parentheses indicate normal range.
Case 1 (TTC)

87 y.o. Japanese man
C.C.: consciousness disturbance, generalized convulsion
P.I.: He had a 30-year history of epilepsy and hypertension treated by a neurologist until 17 months previously. He was barely able to walk indoors, had not been eating properly recently. On a hot summer morning of admission, his son found him immobile in the bathroom. His son called an ambulance because the patient gradually became unresponsive and had a convulsion.
Physical Examination

Consciousness  GCS 6PT, pulse 160-200bpm,
B.P. 110/43mmHg,
B.T. 41.2°C, SpO2 96%( O2 9L mask inhalation)
Skin & tongue: dry
Chest: unremarkable
Abdomen: unremarkable except operation scar
No peripheral edema
Laboratory data

1. CBC: WBC 16,500, RBC 432x104, Hb 15.5, Htc 42.5, Plat 17.7x104
2. Serum Chemistry: T.prot 7.1g/dl, Alb 3.9 g/dl, GOT 82U/L, GPT 38 U/L, LDH 444U/L, Al-P 171U/L, γ-GTP 109U/L, CPK 134U/L, BUN 38mg/dl, Cr 1.88mg/dl, UA 12.4mg/dl, Na 126mEq/L, K 4.2mEq/L, Ca 8.9mg/dl, BS 356 mg/dl, PT(INR) 1.15, APTT 28.0sec, fibrinogen 352mg/dl, CRP 1.37mg/dl
3. Arterial blood gas: pH 7.427, Po2 94.4 mmHg, Pco2 21.7 mmHg, BE -7.8mM/L, Sat O2 96%, AG 21.3mM/L
4. ECG: wide QRS tachycardia, superior axis, atypical CRBBB pattern
5. Chest X-ray: cardiomegaly without pulmonary edema
ECG on admission
Initial Management

• Vigorous cooling:
  2L cold normal saline infusion, surface cooling with ice pack
• Intravenous Lidocaine  50mg & Magnesium sulfate 2.46g
• Intubation, Sedation with intravenous propofol
ECG after lidocaine and Mg
Management in ICU

• Continue evaporative cooling techniques
• Body temperature 37.5°C 4 hours later
• Fell into shock state after conversion to af
  ➡ drip infusion of NAd(0.3μg/kg/min) keeping BP >90mmHg
• Drip infusion of Heparin(500U/h) to prevent thrombus formation
## Serial Laboratory Data

<table>
<thead>
<tr>
<th></th>
<th>DAY1</th>
<th>DAY2</th>
<th>DAY3</th>
<th>DAY8</th>
<th>DAY14</th>
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<tr>
<td>WBC</td>
<td>16500</td>
<td>21400</td>
<td>17300</td>
<td>12400</td>
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<td>Plat(x104)</td>
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<td>4.4</td>
<td>5.8</td>
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<tr>
<td>INR</td>
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<td>1.32</td>
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<td>APTT(sec)</td>
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<td>46.8</td>
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<td>GOT(U/L)</td>
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<td>7521</td>
<td>2626</td>
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<td>223</td>
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<tr>
<td>GPT(U/L)</td>
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<td>2636</td>
<td>1926</td>
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<td>389</td>
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<tr>
<td>LDH(U/L)</td>
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<td>5321</td>
<td>953</td>
<td>501</td>
<td>404</td>
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<tr>
<td>CPK(U/L)</td>
<td>134</td>
<td>4154</td>
<td>3866</td>
<td>1378</td>
<td>182</td>
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<tr>
<td>Cr(mg/dl)</td>
<td>1.88</td>
<td>1.63</td>
<td>1.14</td>
<td>0.79</td>
<td>0.58</td>
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<tr>
<td>UA(mg/dl)</td>
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<td>11.7</td>
<td>8.6</td>
<td>4.4</td>
<td>3.3</td>
</tr>
<tr>
<td>CRP(mg/dl)</td>
<td>1.37</td>
<td>3.61</td>
<td>2.66</td>
<td>3.38</td>
<td>0.83</td>
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</table>
ECG on the next day
UCG  day2
Coronary CT

RCA

LAD

LCX
Clinical course

• Stable hemodynamics after tapering NAd
  ➔ given carvedilol(2.5mg/day) and enalapril(2.5mg/day)
• No recurrence of tachycardia
• Recovered consciousness without neurological deficit on the day 4
• Rhabdomyolysis, DIC: treated without complication
• Complete recovery of LV wall motion on the day 14
UCG after recovery
Stress-induced (Takotsubo) cardiomyopathy

- First report by Japanese doctors in 1985
- Named after Japanese octopus trap
Clinical features

Usually occurs in postmenopausal women
Trigger: Emotional stress mostly in women
   Physical stress mostly in men
Common symptom: chest pain, chest discomfort, dyspnea
Typical time course of ECG in TTC

On admission 2 days 7 days 10 days
Diagnosis

Mayo clinic criteria
1) Transient hypokinesis, akinesis, or dyskinesis of the left ventricular mid segments with or without apical involvement; the regional wall motion abnormalities extend beyond a single epicardial vascular distribution; a stressful trigger is often, but not always, present
2) Absence of obstructive coronary disease or angiographic evidence of acute plaque rupture
3) New electrocardiographic abnormalities (either ST-segment elevation and/or T-wave inversion) or modest elevation in cardiac troponin
4) Absence of pheochromocytoma, myocarditis
Pathophysiology

1) Vasospasm of coronary arteries
2) Disturbance of the microcirculation
3) Catecholamine toxicity
4) Obstruction of the LVOT
5) Estrogen deficiency
Complication and Management

- Cardiogenic shock (6.5%), congestive heart failure (3.8%)
  - inotropic agent, intra-aortic balloon pumping
- Apical thrombus formation, stroke
  - Consider anticoagulation to prevent thrombus formation
- Left ventricular rupture
- Ventricular tachycardia (1.6%), ventricular fibrillation, TdP
  - Immediate cardioversion, correct other factors causing QT interval prolongation
- Persistent left ventricular wall motion abnormality
  - β-blocker, ACE-I?
LVOTO & MR in TTC
Complication and Management

• Cardiogenic shock (6.5%), congestive heart failure (3.8%)
  ➡ inotropic agent, intra-aortic balloon pumping
• Apical thrombus formation, stroke
  ➡ Consider anticoagulation to prevent thrombus formation
• Left ventricular rupture
• Ventricular tachycardia (1.6%), ventricular fibrillation, TdP
  ➡ Immediate cardioversion, correct other factors causing QT interval prolongation
• Persistent left ventricular wall motion abnormality
  ➡ β-blocker, ACE-I?
Prognosis

• Overall favorable outcome, almost complete recovery in 96%
• In hospital mortality 1.1-2%, recurrence rate 11.4%

AA Elesber et al, JACC 50:2007
Case 2 (AMI)

Case: 67 years old, Japanese female
C.C.: lethargy, vomiting, abdominal pain
P.I.: She has no medical or health check history. She had lost appetite and felt lethargy recently. On the day of admission in July, she had been working outside from the morning. In the afternoon, she was transferred to our hospital for fever, vomiting and abdominal pain.
P.H.: none
Physical exam.: consciousness , BT 38.8°C, pulse 48bpm reg, BP 124/88, chest & abdomen; unremarkable
CAG after PCI

RCA

LCA

POST

POST
Pathology of plaque rupture
Conclusion

• Heat-stroke is a form of hyperthermia associated with a systemic inflammatory response leading to a syndrome of multi-organ dysfunction, accompanied by considerable increase in morbidity and mortality.

• Systemic inflammation, coagulopathy, and increased level of catecholamine in heat stroke may be related to development of cardiovascular abnormality.

• Cardiovascular events might contribute significantly to mortality in patients with heat stroke.
Take home message

• Heat stroke can cause multiple organ failure and the presentation of circulatory failure in heat stroke may be the sign of myocardial dysfunction.

• To distinguish acute coronary syndrome and stress-induced cardiomyopathy, both of which could be evoked by heat stroke, the evaluation of coronary artery is necessary.

• Stress-induced cardiomyopathy may cause lethal arrhythmia or circulatory collapse in acute phase.

• Invasive circulatory monitoring is recommended in the patients with severe heat stroke.
Department of Cardiology

Staff: medical doctors 10, clinical engineers 7, Nurses
ICU: 10 beds, Cardiology ward: 54 beds
CT: 320 row area detector (Toshiba)
MRI: 2
Echocardiographic machine: 5
Cardiac catheterization laboratory: 2 rooms
(Cineangiogram: Toshiba: biplane 1, single plane 1)
IABP 2 (+α)、PCPS 2、IVUS 、OCT
Respirator: 12
CHDF 3 (HD10 beds)
SAS related: PSG, CPAP, ASV
Heat Illnesses

Heat related illnesses:
  by exposure without alteration of hypothalamic thermoregulation

Fever:
  by changes to the hypothalamic set point  by pyrogenic condition

<Types of Heat illnesses>
Heat edema, Heat rash, Heat cramps
Heat tetany, Heat syncope, Heat exhaustion
Heat stroke
Heat stroke

<Risk factor>
Environmental factors
Medications
Drug use
Compromised health status (elderly, cardiovascular disease)
Genetic conditions
### Differential Diagnosis in hyperthermia

<table>
<thead>
<tr>
<th>Category</th>
<th>Conditions</th>
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<tbody>
<tr>
<td><strong>Endocrine</strong></td>
<td>Pheochromocytoma, Thyroid storm</td>
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<tr>
<td><strong>Infectious</strong></td>
<td>Brain abscess, Encephalitis, Meningitis</td>
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<tr>
<td></td>
<td>Malaria, Sepsis, Tetanus, Typhoid fever</td>
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<tr>
<td><strong>Neurologic</strong></td>
<td>CVA, Seizures</td>
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<td><strong>Toxicological</strong></td>
<td>Alcohol withdrawal, Anticholinergic toxidromes</td>
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<td>Aspirin overdose, Malignant hyperthermia</td>
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<td>MAO inhibitors, Malignant syndrome,</td>
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<td>Serotonin syndrome</td>
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</table>
**Innate immune Cytokine response**

**Stress-induced Cytokine response**

**TLRs**

- ↑ TLR2
- ↓ TLR4
- ↑ TNFα
- ↑ IL-1β

**Hyperthermia/protein stress**

- HSF → HSP72
- SAPK → C-fos, c-jun

- ↔ TLR2
- ↑ IL-6
- ↑ IL-10

- ↑ IL-6
- ↑ IL-10

- ↓ TNFα
- ↓ IL-1β
Prevention

1. Assessment of environmental heat safety
   Wet bulb globe temperature (WBGT index)
   Equation: heat, humidity, ambient temperature, wind, reflected heat,

2. Good physical conditioning

3. Acclimatization
Acclimatization

Takes several weeks

• Enhancement of cardiovascular performance
• Activation of the renin-angiotensin-aldosterone axis
• Increase in the capacity to secrete sweat
• Salt conservation by the sweat glands and kidneys
• Expansion of plasma volume
• Increase in the glomerular filtration rate
• Increase in the resistance to exertional rhabdomyolysis
Management of heat stroke

1. Out of hospital
Measure the patient’s core temperature
If >40°C
   → move the patient to a cooler place, remove clothing, external cooling(cold pack, fanning, spraying of the skin with water)
Clear the airway, oxygen at 4L/min, isotonic crystal(normal saline)
Transfer to the emergency department
Management of heat stroke

2. In hospital
   <Cooling period>
   Hyperthermia $\rightarrow$ continue cooling
   Seizures $\rightarrow$ Give benzodiazepines
   Respiratory failure $\rightarrow$ consider intubation
   Hypotension $\rightarrow$ Administer fluids (Rehydration), vasopressors, monitoring central venous pressures
   Rhabdomyolysis $\rightarrow$ Volume expansion with normal saline, intravenous furosemide, mannitol,
   sodium bicarbonate
   Monitor serum potassium calcium, treat hyperkalemia
   <After cooling>
   Multi-organ dysfunction: supportive therapy
Methods of cooling

1) Water immersion therapy
   cooling rate: 0.12-0.35°C/min in ice water (<3°C)
   0.04-0.25°C in cold water (>8°C)
   until core temperature reaches 38.8-38.6°C
2) Mist and fan technique
   cooling rate: 0.05-0.14°C/min
3) Ice pack and internal cooling
   Ice pack on the groin, axillae, neck, head
   gastric, bladder, rectal lavage
4) Cooling blanket
5) Intravascular cooling device (Cool line or Icy catheter with Coolgard system)
Case 1 (TTC)

P.H.: 27y.o. colon volvulus, Epilepsy & HTN, leg phlegmon
Medication: none
L.H.: alcohol 50mg/day, non-smoker

Lived in a house without air-conditioning
Laboratory Data

1. CBC: WBC 16400, RBC 479x10^4, Hb 14.8, Htc 40.2, Plat 15.3x10^4
2. Serum Chemistry: T.prot 7.1g/dl, Alb 3.7g/dl, GOT 341U/L, GPT 139 U/L, LDH 973U/L, Al-P 315U/L, γ-GTP 82U/L, CPK 2966U/L(CPK-MB317) BUN 24mg/dl, Cr 2.0mg/dl, UA 8.9mg/dl, Na 126mEq/L, K 6.1mEq/L, BS 667mg/dl, PT(INR) 1.06, APTT 29.7sec, CRP 0.54mg/dl
3. Arterial blood gas(O2 Mask 10L): pH 7.15, Po2 97.4mmHg, Pco2 24.7 mmHg, Hco3 8.7mM/L, BE -18.9mM/L, Sat O2 95.0%, AG 15.7mM/L
4. ECG: Sinus tachycardia, Complete A-V block, q wave & ST elevation in Ⅱ, Ⅲ,aVF
5. Chest X-ray: cardiomegaly and pulmonary congestion