The Hong Kong-Zhuhai-Macao Bridge (HZM bridge) is located at the entrance of the Pearl River, connecting three major cities in the south coast of China (namely, Hong Kong, Zhuhai, and Macao). This ambitious project is the longest bridge-tunnel combination in the world with a total length of 49.97 km consisting of three navigable bridges, two artificial islands, and one fully submerged tunnel. The longest bridge span crossing the Qingzhou Waterway is designed as a cable-stayed bridge with a total span of 458 m. To ensure the safety of the bridge which is designed to have a service life of 120 years, a multi-level, intelligent monitoring system is designed to monitor critical details on the bridge. On the first tier of the system design is a wireless sensor platform to track the structural performance of the weld joints of U-ribs and orthotropic steel decks of the box girder. Next, a base station is used to establish a data transmission subnet on the second-tier of the system. Finally, measurement data is aggregated and analyzed on the third-tier of the proposed multi-tier framework to provide bridge managers a means of assessing the condition of critical bridge details. A typical segment of the steel box girder of HZM bridge is made in the laboratory for experimental testing on the weld root of the orthotropic steel decks. Strain gauges are attached to the U-ribs area to measure the strain values responding to the cyclic loadings with various amplitudes. In addition, a graphic user-friendly interface is tailored to reflect the monitoring data and analysis results to assistant owners and managers for quantitative assess the structural status.